Report Against Acupuncture For Anesthesia Stirs Debate

Medical Tribune World Service

FLORENCE, ITALY—A straightforward denial that acupuncture provides effective anesthesia during surgery in the Western sense of the concept was delivered at the First World Congress on Pain by Dr. Arthur Taub of the department of anesthesiology, Yale University Medical School. He termed acupuncture anesthesia "natural surgery" in an analogy with "natural childbirth," in which reduction of pain is produced in selected individuals by indoctrination combined with social motivation.

Instances where no pain is reported are "anecdotal evidence" of the kind which can also "be gathered about patients who have undergone major surgery for various reasons without any local or narcotic analgesic or needle anesthesia whatever and have denied pain," he said, and can reasonably be attributed to the placebo effect.

Dr. Taub, who specializes in pain research, based his conclusions on observations during a visit to China in May, 1974 (as part of a group of ten American experts) designed specifically to study acupuncture anesthesia.

Acupuncture is not widely used as anesthesia in surgery in China, Dr. Taub pointed out. On the contrary, local, regional or general anesthesia is employed in about 90 per cent of cases, general anesthesia being least favored since sleep and coma are associated in popular thought with the departure of the soul from the body. Patients like to be awake during surgery and Chinese physicians do not have extensive experience with general anesthesia.

At Peking Medical College teaching hospital, operation is performed under acupuncture anesthesia on patient with cancer of the cardia and lower esophagus. Three needles were inserted at points on the left ear and forearm.

Where acupuncture is used, he continued, it is on an experimental basis in major surgical centers where trained anesthesiologic backup is available. It is never used in emergency procedures or poor risk patients and very rarely in juveniles. It is essentially voluntary and patients must be in good health and emotionally stable, "that is, capable of lying motionless, awake, on an operating table for several hours."

Patients Premedicated

Patients selected for acupuncture anesthesia usually receive premedication with barbiturates (up to 500 mg of phenobarbital), narcotic agents (50-100 mg of meperidine I.V.) which may be repeated every two hours during surgery, and sedating agents, Dr. Taub said. Local anesthesia is an integral part of the technique, and may be used for incision through and manipulation of fascia, pleura and peritoneum, viscera and sometimes skin.

Dr. Taub further took issue with official Chinese criteria of success. "Acupuncture 'anesthesia' neither produces 'anesthesia' nor 'analgesia' in the conventional sense," he said. According to the classification system used in Shanghai, he explained, grade I, or an "excellent" effect, allows for "slight pain" and the use of intravenous meperidine and local anesthesia.

Grade II, or good, permits "occasional light groans," changes in blood pressure and pulse and respiration rates, meperidine and local anesthesia. Grade III, or "moderate" success, permits "obvious" pain and "obvious" changes, and increased meperidine as well as "moderate" local anesthesia.

All three grades are considered effective in China, whereas only a portion of grade I would pass the test in the U.S., Dr. Taub pointed out.

Using as an example the statistics published by the Shanghai Acupuncture Anesthesia Coordinating Group in 1973 for 656 cases of pulmonary resection in which acupuncture anesthesia was used, he noted that 161 were rated grade I; 171 grade II and 346 grade III; while 23 fell into grade IV. The "effective" rate was reported as

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Med Trib 44

Medical Tribune

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and Medical News

Vol. 16, No. 44 *world news of medicine and its practice—fast, accurate, complete* Wednesday, December 17, 1975

Editorial

Congratulations

MEDICAL TRIBUNE EXTENDS CONGRATULATIONS to the key officials of the FDA for a landmark public health decision—the labeling of alcoholic beverages under FDA control. The action of Commissioner Alexander M. Schmidt, the physician who heads FDA, Dr. Richard Crout, its Director of the Bureau of Drugs, and Mr. Sam Fine, Associate Commissioner for Compliance of the FDA, introduces logic as well as consistency, proper public health perspectives and priorities into food and drug regulation. It also demonstrates that there are unselfish officials in our health bureaucracy who can place the interest of the public and the national health ahead of personal ambition and job security, ahead of political of bureaucratic expediency.

...Lest We Celebrate Prematurely...

BEFORE WE CELEBRATE PREMATURELY, let us recognize that "the chips are down." In view of the history or tokenism in health

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Current Opinion

Our Readers Write about the President's Cold, Dr. Lasagna's Letter, and Dr. Sackler's View

MEDICAL TRIBUNE *has been deluged with letters from physicians in response to Dr. Lasagna's letter and Dr. Sackler's column (Nov. 19) pointing out that Dr. William Lukash treated President Ford's cold with an antibiotic while FDA and HEW physicians indict practicing physicians for doing just what Dr. Lukash did.*

Dr. Lasagna's letter pointed out most patients do not visit physicians for common colds but treat them themselves—and come to the physician only when secondary bacterial complications have set in. Dr. Lasagna's letter is reprinted again on page 19. Responding physicians offered the following opinions:

• Thank you for the most interesting yet controversial aspect of the President's recent cold.

WILLIAM M. LUKASH, M.D.
Rear Admiral, MC, USN
Physician to the President
The White House
Washington, D.C.

• Dr. Lasagna is absolutely right!

Personally, I have never prescribed an antibiotic for a "cold."

Complications of a cold such as bronchitis with purulent sputum, or patients with a history of rheumatic fever, nephritis, or previous streptococcus if there is an accompanying acute pharyngitis, definitely yes.

EDWARD W. NICKLAS, M.D.
Washington, D.C.

• I agree wholeheartedly with Dr. Lasagna's letter and Dr. Sackler's comments on antibiotic prescribing for "colds." By the time the patient comes to see the physician with his cold, five days or more have gone by and the secondary bacterial invaders have come in and are causing complications, which if not treated with antibiotics may well become more severe.

Over the past 25 years, when my better judgment has been over-ruled by epistles from the FDA or HEW and other academic sources, I have given

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Doctors Cited for Failure To Biopsy Early Breast Ca

Medical Tribune Report

SAN FRANCISCO—Although more cancers are being detected at an early stage by combined breast-screening modalities, many doctors reportedly fail to biopsy patients with "clinically occult" radiographic evidence of early disease.

Consequently, Dr. Gordon F. Schwartz, Associate Professor of Surgery at Jefferson Medical School in Philadelphia and Director of the Breast Diagnostic Center (BDC) has recommended devoting "more efforts at educational programs among the medical profession, demonstrating the value of these ancillary techniques of diagnosis."

Using thermography, mammography, and clinical examination, the BDC has since 1973 found 106 new cancers in 16,345 examinations of 13,907 asymptomatic, self-referred

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making rounds at press time

NEW YEAR'S DAY may find Suburban Hosp. in Bethesda, Md., without 24 obstetrician-gynecologists. They've voted to quit and take pts. elsewhere if hosp. acts on plan to close OB unit. Dr. J. Lukasik, OB staff head, says Suburban would cease to be a community hospital if unit is dropped. Hosp. claims unit uses only 10 of 31 beds and pts. could be better served in regional center. Trouble is, says Dr. Lukasik, there's no regional center.

Senator Kennedy Charges

FDA 'Doesn't Work,' Should Be Split into Separate Agencies

By NATHAN HORWITZ
Medical Tribune Staff

NEW ORLEANS—Plans for a sweeping legislative overhaul of the Food and Drug Administration that would divide it into two agencies—one exclusively responsible for supervision of drugs, the other over foods and cosmetics—were announced here by Sen. Edward M. Kennedy (D., Mass.).

The Senator, who will introduce his proposed legislation in this session of Congress, said the FDA as now constituted simply "doesn't work." In one of the harshest criticisms of the agency yet made by a national figure, Mr. Kennedy charged the FDA is "understaffed, underfunded, overextended" and lacking in adequate scientific know-how to do its job. It delays approval of useful drugs and allows its scientific advisory committees to be used as "rubber stamps" for staff decisions, the

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FDA Chief Dr. Alexander M. Schmidt explains plans to speed drug trials and follow-up. Changes would affect major test procedures.

Atherosclerotic Plaque Reduced Dramatically by Cholestyramine

Medical Tribune Report

ANAHEIM, CALIF.—Cholestyramine has produced "dramatic" regressions of severe atheromatous lesions in primates with experimentally induced atherosclerosis, a University of Chicago team has reported.

The drug was most effective when given in combination with a low-fat, low-cholesterol diet, but even when combined with an atherogenic diet it produced "some evidence of regression" of the atherosclerotic plaques, Dr. Robert W. Wissler, Donald N. Pritzker Professor of Pathology, told the American Heart Association here.

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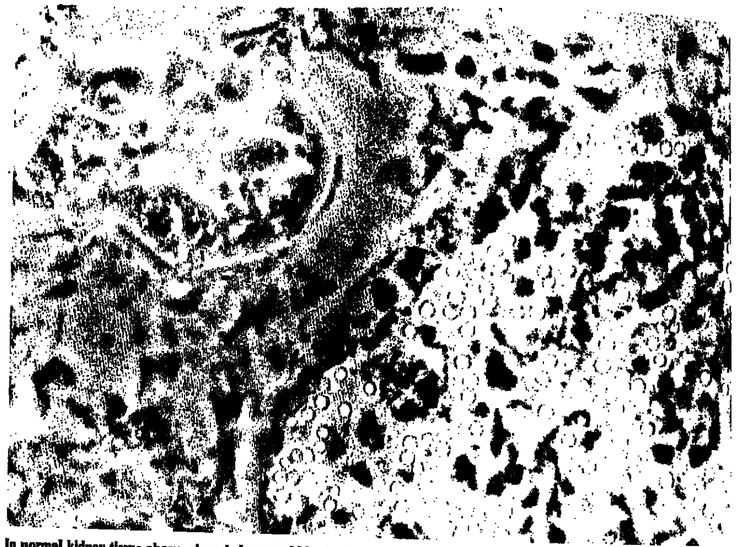
'B' Fragment Receptors Identified in Kidney

By MICHAEL HERRING
Medical Tribune Staff

BETHESDA, MD.—Specific receptors for the "b" fragment of the third component of complement (C3b) have been identified in the kidney's glomerulus by a team of National Institute of Allergy and Infectious Diseases (NIAID) scientists, the institute recently reported.

The finding may lead to the development of immunotherapy against renal diseases such as glomerulonephritis, Dr. Michael Gelfand told MEDICAL TRIBUNE. Dr. Gelfand is Co-Director of the Hemodialysis Unit at Georgetown University Medical Center in Washington, D.C., and a guest worker at NIAID.

"If the receptor indeed mediates immune-complex renal disease, and if there are a finite number of receptors, then one can envision producing a molecule that is structurally similar to the pathogenetic C3b molecule, one that would occupy the glomerular receptor site, but not activate subsequent complement components," Dr. Gelfand explained.



In normal kidney tissue above, ringed sheep red blood cells, coated with C3 (complement) and antibody, adhere only to clusters of blood vessels in portion of glomerulus shown at right. Glomerular receptors apparently bind the "b" fragment of C3, leading to renal diseases such as glomerulonephritis. Future immunotherapy may entail blocking receptors.

Complement Cascade

C3b, he added, is number three in a series of "circulating protein" interactions leading to a complement component with cell- and tissue-destroying properties. "The complement cascade is comparable to the clotting mechanism," Dr. Gelfand said. "Or think of a house of cards. Once the first component is activated, it sets off the next, which in turn sets off the third and so on.

"Antigen-antibody complexes can precipitate the complement cascade. This is the case in immune-complex or antigen-antibody-complex renal diseases, such as poststreptococcal glomerulonephritis or systemic lupus erythematosus. When the protein reaches the C3b stage, it seems to be bound by the renal receptors."

The "cascade" reaction continues from there, Dr. Gelfand said, until a lytic complement protein is produced, causing loss of tissue and blood supply.

To demonstrate these receptors, Dr. Gelfand and his NIAID colleagues Drs. Michael Frank and Ira Green exposed sections of normal human kidney tissue to "indicator sheep red blood cells." Only those sheep cells coated with antibody against the cells plus C3 adhered to the glomeruli of these sections, Dr. Gelfand said.

Sheep red blood cells coated with the same antibody and other components of the complement system did not bind to the tissue. The investigators also found that cells adhered only to the glomeruli, and not other areas of the kidney section.

Further work revealed that only those coated sheep red blood cells containing the "b" fragment of the C3 protein would bind with the glomeruli. "The 'b' fragment is the active portion of the third component—that part that actually binds with the receptor," Dr. Gelfand told MEDICAL TRIBUNE.

"We've also examined a one-day-old child who died of nonrenal causes and had apparently normal kidneys, and found similar evidence for the presence of renal receptors. So it seems that it's natural to have them from birth," he said.

While it appears conclusive that receptors for C3b do exist, Dr. Gelfand stressed that extrapolations of the findings are preliminary, and that further research is required to pinpoint the exact site of receptors and develop appropriate immunotherapy.

Dr. Frank is Chief, NIAID Laboratory of Clinical Investigation, and Dr. Green is Senior Investigator, NIAID Laboratory of Immunology.

Child's Exploratory Behavior Impaired by Malnutrition

Medical Tribune Report

ITHACA, N. Y.—Research at Cornell University suggests that prenatal and neonatal malnutrition do not impair intellectual development by actual physical damage to brain cells, but rather by preventing the child from learning certain kinds of information, David A. Levitsky, Ph.D., of the university's division of nutritional sciences, told the Cornell Conference on Malnutrition and Behavior.

Malnutrition seems to delay eye-muscle coordination in the young and to increase maternal protectiveness, both of which tend to depress the child's environmental curiosity and to inhibit exploratory behavior, Dr. Levitsky said.

Radiotherapy Seen Not Depressing Immunity

Medical Tribune Report

SAN FRANCISCO—Though radiotherapy may cause some short term depression of cell mediated immunity, it apparently has no late or long-term effects on either cell mediated or humoral immunity. That was the conclusion reached by Dr. Martin Halili and associates at Albert Einstein College of Medicine after a prospective, three-year study of 52 patients.

Reporting here at the American Society of Therapeutic Radiologists, Dr. Halili said the study showed that large field irradiation had no late effect on either cell mediated immunity as determined both by skin reactivity to DNCB (2-4 dinitrochlorobenzene) and by the absolute lymphocyte count, or on the humoral circulating immunoglobulins.

There has been some controversy about the short-term effect of local irradiation on the immune system, he said. Several investigators have found a depression of in vitro lymphocyte transformation shortly after radiotherapy plus depression of the absolute lymphocyte count. Others, Dr. Halili noted, have not found a decrease in delayed hypersensitivity using in vivo tests.

But, he said, "the competence of the immune system is critical in achieving a cure of cancer. Any treatment that has a harmful effect on this system may adversely affect survival."

Therefore, he said, he undertook the study to ascertain what, if any, long-term effects there might be. Patients with gynecologic malignancies were studied because they were treated with large field irradiation. This would be more likely to depress the immune system than the small field treatment used for head and neck tumors, he explained.

The cell-mediated immunity was evaluated by skin reactivity to DNCB in patients who were treated by radical radiotherapy alone or by radiotherapy plus surgery, and who are alive and free of disease three years afterwards. All 52 patients received at least 4,000 rads to a minimum field size of 15 by 15 cm.

Croton Oil Reaction

At the time of the DNCB challenge, the patients were also tested with 10% croton oil to determine competence of the inflammatory response. A white blood cell count calculated absolute lymphocyte count, and quantitative serum immunoglobulins were obtained by immunodiffusion test, Dr. Halili said.

He found that 87% of the patients were DNCB reactive and 85% were croton oil reactive. "This is higher than in those tested prior to radiotherapy in a previous study and approaches that of a normal population where 90 to 96% will be DNCB reactive," Dr. Halili noted.

He found also that white blood cell count and absolute lymphocyte count were within the normal range, and that the serum immunoglobulins (IgA, IgM, and IgG) evaluated in 22 patients were also within the normal range.

He did find, he added, that cell mediated immunity was affected by age and that the response to DNCB was affected by the strength of the challenge dose. Thus, the overall reactivity for a 100 microgram challenge dose was 87%, for the 50 microgram dose it was 65%, and for the 25 microgram dose it was 44%. Similarly, there was a decrease in the number of positive DNCB reactors as the age increased, despite the size of the challenge dose, Dr. Halili said.

Cancer Gene 'Mapped' on Tumor Virus

By FRANCES GOODNIGHT
Medical Tribune Staff

COPENHAGEN, DENMARK—An essential step in understanding how viruses induce cancer has been achieved by investigators at the University of California in Berkeley, who reported here that they have "mapped" on a tumor virus molecule the precise location of the gene that causes cells to become malignant.

The research team also determined the location of the gene that controls formation of the protein envelope surrounding the virus particle.

Their work, described at the Seventh International Symposium on Comparative Leukemia Research, is believed to be the first such gene mapping in a virus that causes naturally occurring forms of animal cancer.

Avian Tumor Viruses Used

The Rous sarcoma virus and other avian tumor viruses were used in the experiments, which were conducted by Peter H. Duesberg, Ph.D., Lu-Hai Wang, and Karen Beemon, Ph.D., with colleagues at the university's virus laboratory.

What led to the mapping was their discovery that some avian sarcoma viruses grown in culture changed by mutation into a "deletion mutant"—one that could still produce a leukemia effect in test animals but was incapable of tranforming normal cells to a cancerous state.

By comparing the original tumor virus with the mutant, the investigators determined that the latter contained about 15% less genetic material. They then broke RNA molecules from both viruses into fragments (oligonucleotides) with an enzyme and subjected them to a "fingerprinting" process designed to separate groups of chemical subunits by their varied properties and electric charges.

The results confirmed the biologic tests, demonstrating that sarcoma-specific fragments in the avian tumor virus were not present in the mutant version, and that the missing fragments constituted about 15% of the total material.

The Berkeley group had established that one end of the sarcoma virus RNA molecule is marked by some 200 adenine units strung together. Since this Poly (A) unit can be tagged by linkage to other units, the investigators again fragmented such tagged RNA molecules and found that the cell-transforming activity was close to the Poly (A) end of the molecule, in a cluster of oligonucleotides that represent the "oncogenesis" gene.

Mapping of the envelope was achieved by similar sophisticated tests, using a mutant sarcoma virus that lacked an outer envelope but retained its ability to transform cells.

Still to be mapped, the investigators noted, are the gene governing the polymerase enzyme responsible for nucleic acid replication and the gene that controls formation of the inner protein coating of the virus.

They now plan to analyze the more complex mammalian cancer viruses, with the goal of spelling out the genetic code of viral segments and finding out how the gene message is carried to the point where normal cell processes are disrupted and malignant changes occur.

Viruses in Leukemia

► An overview of symposium reports dealing with new concepts of the role of viruses in human leukemia was subsequently presented in New Orleans to the Leukemia Society of America by David S. Yohn, Ph.D., director of the Ohio State University Cancer Research Center, Columbus.

Dr. Yohn cited morphologic, immunologic, and biochemical evidence for human RNA leukemia viruses and concluded: "The evidence is overwhelming that RNA tumor viruses are associated with human leukemia, probably etiologically."

But it is equally evident, the investigator declared, that no *proven* human leukemia virus has as yet been isolated.

He summed up two predictions: In the next five years, trials will be carried out in mice and cats to determine whether pure vaccines prepared from glycoprotein (gp 69/70) antigens of known RNA tumor viruses, such as feline leukemia virus, murine leukemia virus, and simian sarcoma virus, will protect these animals from naturally occurring virus-induced leukemia.

If such animal trials are successful, by the end of the century similar trials will be underway in patients. The studies will be carried out with purified gp 69/70 antigens known to cross-react with human leukemia cells.

And it is "just possible that a preventive vaccine against human leukemia will be established by the year 2000," Dr. Yohn said.

Leukemia Therapy

► Immunotherapy combined with chemotherapy in clinical trials in patients with acute myelocytic leukemia produced longer remission durations than did chemotherapy alone, according to J. George Bekesi, Ph.D., and colleagues of Mount Sinai School of Medicine, New York.

Patients in whom remission had been achieved by cytosine arabinoside and daunorubicin were allocated to two groups for the trials. Both received cyclical maintenance chemotherapy every four weeks. Patients randomized to receive immunotherapy were also given neuraminidase-treated allogenic myeloblasts, injected intradermally at monthly intervals in approximately 40 sites in different drainage areas.

Of 10 patients who had received previous antileukemia chemotherapy, the six immunized patients had more than twice the remission duration of the four controls, the investigators said.

Among 18 patients previously untreated, the median remission duration for nine patients on chemotherapy alone was 22 weeks. In contrast, six of the nine patients receiving the combined therapies remain in remission from 68 to 115 weeks.

Drug Selection

► A biochemical test that may help physicians determine which of two recommended drugs to select for a given patient with acute myelogenous leukemia (AML) was described by Dr. Bruce A. Chabner, of the National Cancer Institute.

The test may also indicate whether or not an AML patient is apt to respond to either of the two agents—cytosine arabinoside (ara-C) and 5-azacytidine (5-aza-C)—and prospective trials of the test are now underway, Dr. Chabner said.

Both drugs have chemical structures similar to naturally occurring nucleosides and thus compete with such nucleosides for enzymes essential to the synthesis of DNA.

In studies of 44 previously untreated AML patients, blast cells were tested for activity of deoxycytidine kinase, the enzyme that activates ara-C; uridine-cytidine kinase, the enzyme thought to activate 5-aza-C; and cytidine deaminase, the enzyme that converts both drugs to an inactive form.

Dr. Chabner and coworkers found that the patients had markedly different potentials for activating or degrading the drugs. Enzyme levels varied independently, with no apparent relationship to the subclass of the leukemia or to sex.

Helmet Laws Seen Lowering Deaths In Cycle Mishaps

Medical Tribune Report

WASHINGTON, D.C.—Laws requiring motorcyclists to wear helmets are reducing fatalities in motorcycle crashes, according to a study conducted by Leon Robertson, senior behavioral scientist for the Insurance Institute for Highway Safety.

The study compared fatal crash involvement rates in eight states (Arizona, Colorado, Idaho, Kansas, Kentucky, Louisiana, Maryland and Minnesota) which adopted helmet laws, with similar states (California, New Mexico, Montana, Iowa, Virginia, Mississippi, West Virginia and Iowa) that had no such laws during a comparable period.

The "average fatal involvement rate for the eight states that enacted helmet use laws declined from more than 10 per 10,000 registered motorcycles the year before the laws' enactments to about seven per 10,000 registered motorcycles, both in the years of enactments and the following years," Mr. Robertson reported. "In contrast, the average fatal involvement rate in the eight matched states that enacted no helmet laws at the time that their comparison state did so remained at about 10 per 10,000 registered motorcycles throughout the period studied."

Next week Dr. Sackler will address the strange problem of "The Three Horsemen of Death—Alcohol, Tobacco and Firearms" being under the jurisdiction of the U.S. Treasury Department.

index

CLINICAL NEWS NOTE: *"[Monkeys treated] with cholestyramine show a substantial decrease in lumenal narrowing as compared to the reference group autopsied at 12 months....With this kind of evaluation, we can say with confidence that we have stopped the progression of coronary and aortic disease . . ."* (Dr. Robert W. Wissler, Professor of Pathology, University of Chicago, Pritzker School of Medicine. See page 1.)

feature index

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Circulation audited by Business Publications Audit of Circulation, Inc.

MEDICAL TRIBUNE is published each Wednesday except on March 31, June 6, June 16, June 30, July 14, July 28, Aug. 11, Aug. 25, Sept. 29, Dec. 1, Dec. 22, Dec. 29, by Medical Tribune, Inc., 880 Third Ave., New York, N.Y., 10022. Controlled circulation postage paid at Vineland, N.J. 08360. Subscription $25.00, Students $7.50.

EDITORIAL CAPSULES

. . . brief summaries of editorials or comments in current medical and scientific journals.

More Work Needed

". . . much more work is needed before acupuncture analgesia can be understood, and . . . such work will require careful attention to measurement procedures. Psychophysical studies have thus far succeeded in demonstrating that the sensory aspects of human pain can be attentuated, to at least a small extent, by electrical acupuncturat stimulation, and that direct behavioral observations of this effect on the part of experimental subjects. The acupuncture puzzle has opened a new frontier to the pain scientist, and study of acupuncture analgesia should help lend the way to a more profound understanding and eventually to better medical control of human pain." *(Editorial, C. Richard Chapman, Ph.D., Anesthesiology 43:501, Nov., 1975)*

Diabetes and the Heart

". . . The annual reported mortality of about 38,000 is thought to be an underestimate and it has recently been suggested that as many as 300,000 diabetic patients die each year. Diabetes has moved recently from eighth to the fifth leading cause of death in the United States . . .

". . . Coronary artery disease accounts for more than half of the deaths in diabetic subjects (with onset after the age of 20) and is thus the most frequent and hazardous risk in the diabetic population. Autopsy studies reveal an increased incidence (and severity) of CAD in the diabetic subject (45 to 70 per cent) when compared to the nondiabetic subject (8 to 30 per cent).

"Several features of CAD in the diabetic subject deserve special emphasis. In the younger diabetic patient (age 20 to 40), clinically significant CAD is quite common, particularly when the duration of diabetes is long. In the mature onset diabetic CAD tends to pursue an accelerated course and may in fact be the presenting clinical picture. The premenopausal diabetic female has a prevalence of CAD equal to, or even exceeding, that of the diabetic male of comparable age. Hypertension is more prevalent in the diabetic subject than in the nondiabetic population. Coronary artery disease is twice as common in the diabetic hypertensive subject (as compared to the nondiabetic hypertensive subject). The rarity of malignant hypertension in the patient with long-standing diabetes and diabetic complications may be related to decreased activity.

"The prevalence, importance, and even the existence of small coronary artery disease in diabetes is unresolved. A recent interesting report of myocardial biopsy in eight diabetic patients with heart failure or angina has revealed intimal arteriolar proliferation in all. *(Editorial, Ralph C. Scott, M.D., Amer. Heart J. 90:283, Sept., 1975)*

TB Problem: 'Little Room for Complacency'

Medical Tribune World Service

MEXICO CITY—At the beginning of the third decade of the chemotherapy era, "little room for complacency is warranted" with respect to the world tuberculosis problem, according to an analysis of trends projected to the year 2,000.

Unanticipated Development

This world-wide projection, presented at the 23rd Conference of the International Union Against Tuberculosis, was developed by the Tuberculosis Control Division of the Center for Disease Control, Atlanta, and is thought to be the first of its kind made for a disease. It embraces the half century period from 1950 to 2,000 and is based on data from at least 60 countries that had information available covering the period 1950-1972.

Continuing reduction in tuberculosis incidence would be a realistic expectation in countries with organized modern public health facilities and adequate fiscal support because effective methods for controlling the disease are available and have been successfully applied for several decades. At the same time, however, an unanticipated development came to the fore: In a few countries and several regions, not only is prevalence of tuberculosis still inordinately high but a plateau in the reduction of incidence is evident. "This suggests," said Anthony M. Lowell, chief of statistics and analysis of CDC's Tuberculosis Control Division, "that diversities of epidemiologic and socioeconomic conditions are important factors in tuberculosis control and that eradication of the disease in many parts of the world by the end of the 20th century is a matter of academic speculation. The present rate of tuberculosis incidence in over 150 countries is 75 per 100,000. I anticipate that without improvement of present conditions, the rate in 1975 will be between 30 and 40 per 100,000, or about half—not good enough to be thinking in terms of eradication."

15 Million Cases

It was estimated from the available prevalence data that there may be 15 to 20 million infectious cases of tuberculosis throughout the world. In some areas of African, Asian, Western Pacific, and South American countries, the reported annual incidence of pulmonary tuberculosis is as high as 250 to 300 cases per 100,000 inhabitants. In a few countries, according to WHO reports, tuberculosis is the leading cause of death from notifiable diseases and in still others it accounts for more deaths than all infectious and parasitic diseases combined.

Extrapulmonary Cases Static

In the United States, the latest data show a reduction in new cases of 2.8% in 1974, confined almost entirely to localities of less than 100,000 population with no significant changes in the larger cities. Practically all reductions were in pulmonary tuberculosis with no change indicated in the number of extrapulmonary cases which has remained static at about 12.8% of all new cases for the last 10 to 15 years. It was pointed out as being of interest that over half the U.S. tuberculosis problem is concentrated in 2,000 counties which demonstrates that it is not characteistic mainly of big cities.

"Generally speaking," Mr. Lowell concluded, "we must be cautious in speculating about the future of tuberculosis as an international health problem but statistical evidence we have been able to gather suggests strongly that in many parts of the world it will continue to be of serious public health concern for several generations."

Narcolepsy: A Neglected Area of Medicine

By ANASTASIA TOUFEXIS
Medical Tribune Staff

NEW YORK—The poodle named Mike staggered around the room. Suddenly his hind legs stiffened. He collapsed on the floor and slept. Mike is one of seven dogs belonging to Stanford University's Sleep Disorders Clinic. Mike has narcolepsy.

As many as 250,000 Americans may have undiagnosed narcolepsy, specialists in sleep disorders believe.

"Sleep disorders are one of medicine's major neglected areas," neurologist Dr. Elliott D. Weitzman told a symposium here on sleep physiology and pathology sponsored by California's Stanford University and New York's Albert Einstein College of Medicine. "Narcolepsy is perhaps the best known and the most dramatic. Undetected it can be the cause of marriages breaking up, difficulties in learning and trouble on the job."

Simple to Recognize

Dr. Weitzman is director of the Sleep-Wake Disorders Unit and chairman of the department of neurology at Montefiore Hospital and Medical Center and Albert Einstein College of Medicine.

Narcolepsy is a chronic, often progressive, potentially disabling disorder with no known cause or cure.

Ironically, although it is rarely diagnosed, it is simple to recognize, according to Dr. William C. Dement, director of the Sleep Disorders Clinic and Laboratory and Professor of Psychiatry at Stanford University in California.

The disorder classically appears at puberty, said the specialists. The two major symptoms are sleep attacks at inappropriate times, such as when driving or working, and cataplectic attacks involving an abrupt loss of voluntary muscle control leading to partial muscle weakness or complete body collapse. Hypnagogic hallucinations, sleep paralysis, and disrupted night-time sleep are also common symptoms.

"The symptoms are so bizarre, they border on the humorous," said Dr. Weitzman. Officials of the American Narcolepsy Association, newly formed in Stanford, Calif. and established as a clearinghouse of information on narcolepsy, recounted personal experiences, including one embarrassing incident involving falling asleep in his spaghetti.

"Narcolepsy is more common than multiple sclerosis," declared William P. Baird, the Association's director, "yet so few doctors are aware of it that an average of more than ten years pass between the first appearance of symptoms and the initial correct diagnosis. Sufferers are often incorrectly treated for a variety of other illnesses or more commonly believed to be just lazy by their friends and even their doctors. The average person who has narcolepsy sees four to five doctors before one finally identifies the illness."

Dr. Dement seconded Mr. Baird's comments. "We have a girl whose symptoms began when she was nine. She's now 16. After the first attacks, her IQ began to drop and eventually she was labeled retarded. Over the years she received psychiatric treatment and was subjected to sophisticated tests, including pneumoencephalogram. We calculated that inappropriate tests and treatment over the seven years cost the family $50,000."

"Usually, a history is sufficient to establish the diagnosis," said Dr. Weitzman. "However in 10 to 20% of the patient population, diagnosis is a problem. In sleep clinics, what we do is take electroencephalograms of daytime naps or all-night sleep. In narcolepsy, the onset of rapid eye movement (REM) sleep occurs at abnormal or inappropriate times. Normal individuals do not have REM sleep during naps. The 24-hour sleep-wake cycle is all mixed up in narcoleptics."

There is no established cause of narcolepsy. "There is no clear evidence that narcolepsy is a psychiatric disease," said the specialists. However, researchers have noted that attacks can be triggered by emotional stress.

Biochemical Imbalance?

There is also speculation that the disorder involves a biochemical imbalance. A predisposition to the illness appears to run in families, they said.

At present, treatment consists of lifelong drug use, primarily with methylphenidate and amphetamines, Dr. Weitzman said. Compounds relieving motor paralysis are also prescribed.

"Tolerance to the drugs is the greatest problem," said Dr. Dement. "It occurs within months or years." Serious side effects of chronic drug use include psychosis, irritability, sexual dysfunction and hypertension.

Investigators have been hampered by the difficulties inherent in human studies, as well as by a lack of money. "It's difficult to examine brain tissue and cerebrospinal fluid in living subjects," Dr. Dement explained.

"We hope to begin research with animals. We've got a colony of seven dogs, including one Doberman, one dachshund and several poodles, with canine narcolepsy. So far the dog is the only animal outside of man that we know has the illness. We've heard stories of an identical syndrome in horses, but this has not been verified."

MDs Seen Failing To Biopsy Early Breast Ca

Continued from page 1

women, Dr. Schwartz said in a report here to the Clinical Congress of the American College of Surgeons.

Of the total examined, 599 women had findings for which biopsy or aspiration was recommended, he said, and 327 of these (58%) actually underwent surgical biopsy. The 106 cancers found represented 32% of all biopsies performed, he noted. While this ratio of biopsies to detected cancers is not high, "the rate in most hospitals is five or six biopsies for each carcinoma encountered."

However, in 90 women with no palpable mass but with suspicious radiographic pictures, Dr. Schwartz said that either the patient herself, or her doctor, refused to go further with biopsy. Almost three-fourths of these patients were advised against biopsy by their doctors, "because they could not palpate 'anything wrong' with the breast," Dr. Schwartz found.

Practitioner Support Needed

In order to be effective, mass screening programs such as the BDC must have the support of educated practitioners who will not ignore radiographic evidence of disease, he stressed.

The rate of six new cancers per 1,000 examinations (slightly less than eight per 1,000 patients screened) was "higher than initially expected according to similar studies." But whether this was due to better screening methods or increased incidence remains in question, Dr. Schwartz said.

More than 45% of all positive findings were clinically occult, he pointed out. "The great majority [i.e., more than 77%] of the carcinomas detected in this program have been extremely early with no evidence of axillary lymph node metastasis." This, he noted, suggests better screening rather than higher rates of disease.

"Survival in those patients with clinically occult lesions should be excellent," Dr. Schwartz also said. "In those patients with clinically occult lesions and negative lymph nodes, the survival should approach 90%, or even higher," but these lesions must be removed promptly, he suggested.

"As a byproduct of our finding of many nonpalpable lesions, we have popularized the technique of locating and excising nonpalpable breast lesions with sacrifice of minimum contiguous normal breast tissue," he said.

Co-authors of the study included Drs. Stephen Feig, Herman Lipshitz, and Arthur Patchefsky.

Firearms Cause Deafness

Medical Tribune Report

WASHINGTON, D.C.—A new government study by physicists Pearl Weissler and Michael Kobal, of the National Bureau of Standards, reports that the noise from most common firearms, especially on a firing range, can cause temporary or permanent deafness in the unprotected marksman.

IN CONSULTATION

What's New and Important in the Management of Asymptomatic Carotid Bruits

The Consultant

DR. JESSE E. THOMPSON

Department ofGeneral Surgery
Baylor University Medical Center
Dallas, Tex.

DURING THE PAST TWO DECADES, it has been clearly established that in many patients with cerebrovascular insufficiency the responsible atherosclerotic occlusions are in the extracranial vasculature. In fact, Hass et al state that 74 % of such patients have at least one significant lesion at a surgically accessible site. It is, therefore, technically feasible to increase cerebral blood flow by surgical means. Carotid endarterectomy is highly effective in the treatment of patients with transient cerebral ischemia, since symptoms are relieved in most instances and the incidence of subsequent strokes is markedly reduced.

The most controversial area in this field concerns the advisability of performing arteriography and surgery on patients with asymptomatic carotid bruits. Asymptomatic subclavian bruits, even with a demonstrated subclavian steal syndrome, do not require operative intervention. The mid-carotid bruit, however, reflecting the presence of atherosclerosis at the common carotid bifurcation is another matter. The majority of such bruits arise from internal carotid plaques, the rest coming from external carotid plaques or other uncommon lesions. The indications for endarterectomy in patients with asymptomatic carotid bruits, however, have not yet been clearly defined.

A safe, simple, and reliable noninvasive screening technique has been needed. Kartchner and his associates have reported the use of the oculoplethysmogram as a noninvasive screening method to determine the significance of carotid bruits. The report of these authors to date has been very encouraging with the OPG giving 91% accurate results when correlated with the arteriogram, a 6% incidence of false-negatives, and a 3% incidence of false-positives.

Do you recommend auscultation of the neck as a routine measure?

Auscultation of the neck for the presence of carotid bruits is an important examination in patients with cerebrovascular insufficiency syndromes. In fact, this should be done in every routine physical examination, especially in patients over the age of 40 and in those with evidence of atherosclerosis elsewhere in the body. The standard 3 cm bell stethoscope remains the most satisfactory one for cervical auscultation.

The differential diagnosis of cervical murmurs includes physiologic murmurs of no significance; venous hum; arteriovenous fistula; angiomatous malformations; intracranial neoplasm; Paget's disease of the skull; fever; anemia; thyrotoxicosis; atherosclerosis of the innominate, subclavian, vertebral and carotid arteries; loops, kinks and fibromuscular dysplasia of the carotid artery; and transmitted cardiac murmurs.

In children and young adults cervical murmurs are of little significance. They are usually heard at the base of the neck and their incidence decreases rapidly with increasing age. Over the age of 40, however, cervical murmurs are much more significant, the carotid bruits being those most commonly encountered.

What distinguishes the carotid bruit?

The most important cervical bruit is the mid-carotid, heard over the carotid bifurcation near the angle of the jaw. It is usually highly localized and disappears quickly as one listens inferiorly. Carotid bruits vary in intensity from soft to very harsh and may be graded from 0 to 4+ on a quantitative basis. They appear when stenosis is 50% or greater and may actually disappear at 85 to 90% stenosis.

A carotid bruit when present is a significant finding in patients with cerebrovascular insufficiency. The controversy arises as to the significance of the bruit in the absence of cerebral symptoms.

How do you consider the asymptomatic bruit?

It does not appear unreasonable to consider the asymptomatic carotid bruit as part of the total picture of cerebrovascular insufficiency rather than an isolated finding on physical examination. The natural history of ischemic thrombotic stroke due to extra-cranial lesions must begin somewhere. It may begin as a plaque at the common carotid bifurcation and its first physical manifestation be an asymptomatic bruit. With time the asymptomatic lesion becomes symptomatic from ulceration and embolization or from impairment of cerebral blood flow. Hopefully the first symptom is a TIA, when therapy can be initiated. At times, however, the first symptom is hemiplegia, especially if a stenotic carotid undergoes acute total occlusion.

Javid et al have studied the natural history of carotid atheromas on serial arteriograms over a period of one to nine years. They noted no change in size of the atheromas in 38% of the lesions studied but found a significant increase in 62% of the atheromas. The increase was greater than 25% per year in 34% of lesions, was less than 25% per year in 20%, while recurrent stenosis or thrombosis occurred in 7.4%.

During the past 18 years my colleagues, Drs. R. Don Patman and Alfred V. Persson, and I have performed more than 1100 carotid endarterectomies for the various syndromes of cerebrovascular insufficiency. During this time we have had the occasion to see a number of patients with asymptomatic carotid bruits. In one series of 119 elective operations upon 84 patients with asymptomatic bruits there has been no operative mortality. General anesthesia was used together with a temporary inlying shunt routinely for cerebral protection. There have been two neurologic deficits associated with operation, both permanent and both mild, an incidence of 1.7%. During long-term follow-up no patient has died of stroke but one patient has had a major stroke and one a mild stroke.

How did this compare with patients who were not operated upon?

For a control series to compare with the surgical series 102 patients with asymptomatic bruits who were not operated upon when the bruit was first detected were followed. There were various reasons for not operating upon these patients when first seen. In the early days of the study it was unclear as to whether they should be operated upon at all. In some patients the bruit was unilateral and very soft. Certain patients did not wish to have arteriography or surgery considered while in others the patients' referring physicians did not wish to have studies performed. The control series has been followed up to 10 years. During this time 55 of the 102 patients have remained asymptomatic—(54%). In 28 (27%) transient cerebral ischemia developed and these patients were operated upon. Nineteen (19) patients (19%) had frank strokes usually without transient ischemic attacks from two days to four years following detection of the bruit. Thus in 47 or 46% of the 102 patients transient ischemia or frank strokes developed during the follow-up period. When a stenotic carotid artery becomes totally occluded there is a significant incidence of acute hemiplegic stroke with its attendant mortality and morbidity.

Javid et al cite their experience with endarterectomy for asmytomatic bruits in 50 patients. Because of the high long-term mortality from causes other than strokes these authors believe that endarterectomy for asymtomatic bruits is inadvisable in hypertensive patients over the age of 65 with a history of myocardial infarction. In younger patients without several risk factors, however, they recommend endarterectomy for severe internal carotid stenosis.

What is the status of cerebral arteriography at present?

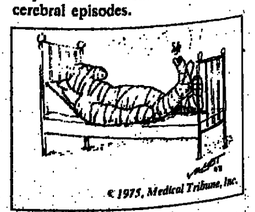
In the final analysis, arteriography is the definitive diagnostic maneuver necessary to establish the origin of a carotid bruit and to determine its significance as a stroke hazard. As cerebral arteriography has become increasingly safer it should be recommended more often for studying patients with asymptomatic carotid bruits.

Arteriography should probably *not* be recommended if the bruit is very soft and unilateral, if other considerations contraindicate surgery even if a significant lesion were found, if other conditions take priority over study of carotid lesions, and in the presence of a negative OPG test. The overall general status of each patient should be considered very carefully before recommending arteriography.

If the arteriograms show a significant atherosclerotic stenosis in the internal carotid artery endartorectomy may be cautiously considered. Specific indications include 1) bilateral stenosis, 2) unilateral stenosis with contralateral occlusion, 3) stenosis in the artery to the dominant hemisphere, 4) known progressive atherosclerotic lesions elsewhere in the peripheral vasculature, especially in younger patients, 5) contemplated major surgery of another sort where a hypotensive episode might well result in a stroke, and 6) an ulcerated atherosclerotic plaque.

Since no unnecessary risks should be taken appropriate measures for cerebral protection must be employed during carotid endarterectomy to avoid producing neurologic deficits. Our recommendation is the routine use of a temporary inlying shunt. Operative mortality should be below 1% and complications no more than 2%.

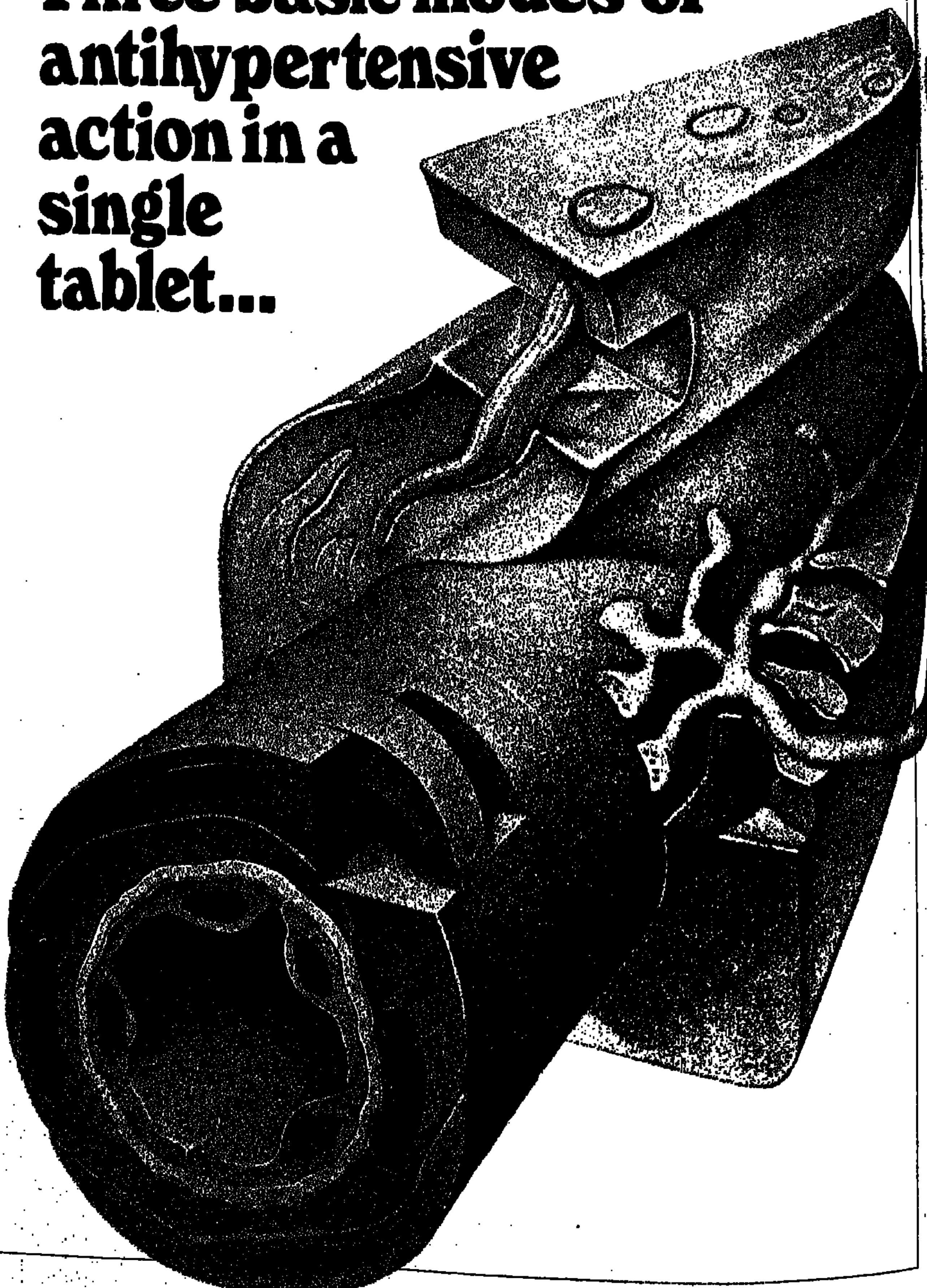
In summary, asymptomatic carotid bruits may originate in the internal carotid artery from atherosclerotic plaques which predispose to strokes in certain individuals over the age of 40. Certain recently developed noninvasive screening tests are helpful in determining the hemodynamic significance of these bruits, which ultimately require arteriography to determine precise diagnosis and significance. If hazardous lesions are demonstrated, carotid endarterectomy may be recommended for selected patients without multiple risk factors to prevent the occurrence of ischemic cerebral episodes.



Next In Consultation

WILLIAM L. HASKELL, PH.D., *Clinical Assistant Professor of Medicine, Cardiology Division, Stanford University School of Medicine, Palo Alto, Calif.*, will discuss what's new and important regarding physical exercise after myocardial infarction, how soon exercise should be undertaken and how to determine additions to the exercise program, the benefits of exercise—and its hazards.

Three basic modes of antihypertensive action in a single tablet...



all the medication many patients need...

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

Current clinical practice stresses the importance of achieving control of basic homeostatic mechanisms as the key to control of high blood pressure.[1]

Indeed, the landmark VA studies utilized three basic drugs to establish control of three homeostatic mechanisms.[2-4] These were control of fluid volume with hydrochlorothiazide, control of sympathetic activity with reserpine, and control of arteriolar tone with hydralazine. The study of 1967 concluded that most hypertensive patients could be successfully controlled with combinations of these basic drugs.[5]

Only Ser-Ap-Es provides control of three basic mechanisms—employing the same antihypertensives used in the VA studies. (In the VA studies, Ser-Ap-Es itself was not used. However, all the components of Ser-Ap-Es were used in varying combinations.)

And when the dosage of each component corresponds to the dosage pre-established by individualized titration, Ser-Ap-Es may prove more convenient and economical. Many patients will need no other medication.

Note: Use Ser-Ap-Es cautiously in patients with advanced renal damage or cerebrovascular accident. Discontinue at first sign of mental depression.

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Ser-Ap-Es®

reserpine 0.1 mg
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WARNING
This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

INDICATIONS
Hypertension. (See box warning.)

CONTRAINDICATIONS
Reserpine: Known hypersensitivity; mental depression (especially with suicidal tendencies); active peptic ulcer; ulcerative colitis; electroconvulsive therapy.

Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.

Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

WARNINGS
Reserpine: Use with extreme caution in patients with a history of mental depression. Discontinue at first sign of despondence, early morning insomnia, loss of appetite, impotence, or self-deprecation. Drug-induced depression may persist for several months after drug withdrawal and may be severe enough to result in suicide.

MAO inhibitors should be avoided or used with extreme caution.

Hydralazine: Hydralazine may produce in a few patients a clinical picture simulating systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefit to risk determination requires continued antihypertensive therapy with this drug. Symptoms and signs usually regress when the drug is discontinued but residua have been detected many years later. Long-term treatment with steroids may be necessary.

CBC's, L.E. cell preparations, and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydralazine or if the patient develops any unexplained signs or symptoms.

A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.

Use MAO inhibitors with caution.

Hydrochlorothiazide: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Usage in Pregnancy
Reserpine: The safety of reserpine for use during pregnancy or lactation has not been established; therefore, the drug should be used in pregnant patients or women of childbearing potential only when, in the judgment of the physician, it is essential to the welfare of the patient. Increased respiratory tract secretions, nasal congestion, cyanosis, and anorexia may occur in neonates and breast-fed infants of reserpine-treated mothers since reserpine crosses the placental barrier and appears in maternal breast milk.

Hydralazine: The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Thiazides cross the placental barrier and appear in cord blood.

Nursing Mothers
Thiazides appear in maternal breast milk.

PRECAUTIONS
Reserpine: Use cautiously in patients with history of peptic ulcer, ulcerative colitis, or gallstones (biliary colic may be precipitated).

Exercise caution when treating hypertensives with renal insufficiency. Use cautiously with digitalis and quinidine.

Intraoperative hypotension has occurred in hypertensive patients receiving rauwolfia preparations, but withdrawal of reserpine does not assure that circulatory instability will not occur in such patients.

Hydralazine: Use cautiously in suspected coronary artery or other cardiovascular disease, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.

Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.

Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver diseases or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS
Reserpine: Gastrointestinal—hypersecretion; nausea; vomiting; anorexia; diarrhea. *Cardiovascular*—angina-like symptoms; arrhythmias (particularly when used concurrently with digitalis or quinidine); bradycardia. *Central Nervous System*—drowsiness; depression; nervousness; paradoxical anxiety; nightmares; rare parkinsonian syndrome and other extrapyramidal tract symptoms; CNS sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, and optic atrophy). *Miscellaneous*—frequently nasal congestion; pruritus; rash; dryness of mouth; dizziness; headache; dyspnea; syncope; epistaxis; purpura and other hematological reactions; impotence or decreased libido; dysuria; muscular aches; conjunctival injection; weight gain; breast engorgement; pseudolactation; gynecomastia; rarely water retention with edema in hypertensive patients.

Hydralazine: Common—headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent*—nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.

Hydrochlorothiazide: Gastrointestinal—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo, paresthesias, headache, xanthopsia. *Dermatologic-Hypersensitivity*—purpura, photosensitivity, rash, urticaria, necrotizing angiitis, Stevens-Johnson syndrome, and other hypersensitivity reactions. *Hematologic*—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. *Cardiovascular*—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. *Other*—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSAGE
As determined by individual titration (see box warning).

Usual dosage is 1 or 2 tablets t.i.d. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by at least 50 percent.

HOW SUPPLIED
Tablets (dark salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 15 mg hydrochlorothiazide; bottles of 30, 60, 100 and 1000.

Consult complete literature before prescribing.

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CIBA

The Only Independent Weekly Medical Newspaper in the U.S.

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...Lest We Celebrate Prematurely...

Continued from page 1

regulation, of hypocrisy in avoidance of real issues, we must be forgiven our skepticism, if not cynicism, as to what will now happen. While we admire the courage of the government officials who now try to move forward as good doctors, good officials and good citizens should do in the public interest, we fear for both their careers and for the outcome of their constructive initiatives.

It is not too hard to predict that legal and/or legislative grounds will be found or provided to nullify an action that is as welcome as it is belated. For 35 years the public has been bamboozled into the belief that substantive actions were being taken in protection of their health.

The public does *not* realize that medicinals, no matter how beneficent in a therapeutic application, would rarely if ever be marketed if they combined the high addictive potential with the carcinogenicity, the cardiac, cerebral and hepatic-toxicity of alcohol.

The public does *not* know that alcohol and tobacco, or either one alone, year in and year out kill more people and do more damage than all other drugs combined and do so to such an extent as to constitute in themselves the major preventable causes of death in the United States, as it does in most "civilized" societies.

How was the public to know the truth and the whole truth about a drug which enslaves over nine million Americans and plagues the lives of scores of millions in their families? Was there a conspiracy of silence? How can one understand the inaction of FDA officials of the past, the lack of adequate and persistent hearings in our houses of Congress, the relative apathy of the editorial writers of even our greatest newspapers and the mass media as a whole?

As long as news and facts of the monumental damage caused by alcohol and tobacco to millions of Americans continues to be a "no-no," so long will we fail to face up to our major *preventable* health problems.

...A Landmark Action

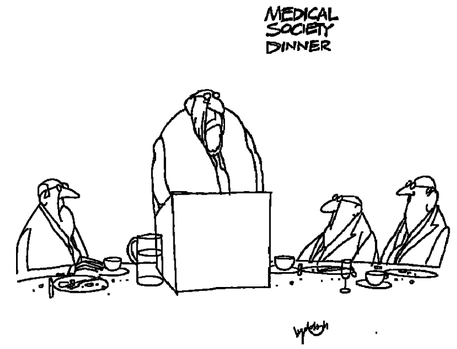
THE PRESENT LANDMARK ACTION of the FDA could be the most important single act of that body in the 35 years since it transferred the liquor-labeling authority to the Bureau of Alcohol, Tobacco and Firearms of the Treasury Department—*if it is not reversed*. It can and it should save more lives, prevent more physical damage, reduce more social derangements than all prior actions of the FDA in respect to all drugs. It can and it should reduce the flood of diversionary attacks on doctors and their drugs and restore true public health perspectives. It can and it should replace the shadow of regulation with the substance of public health protection in respect to *all food and drugs*.

Regulation must encompass not only safe and effective medications and foods but also these most toxic of substances which, through political and legislative legerdemain, have been classified illogically, unscientifically and dishonestly as a "food," in the case of alcohol, and as an "agricultural product" in the case of tobacco. There has been an idiocy in respect to the drug hysteria that has been whipped up about marijuana and medicinals—unless it was used as a "cover" for the virtual default of protective government action in respect to alcohol and tobacco, the two major problems of drug addiction and drug damage, somatic, psychic, and social.

We have noted editorially that the major contributions of recent Republican Administrations in the health field was the upgrading of the health agencies leadership and manpower with the appointments of men of brilliance and proven achievement, as Dr. Theodore Cooper, Assistant Secretary for Health; men of competence and proven background such as Dr. Alexander M. Schmidt, the FDA Commissioner; Dr. Richard Crout, Director of the Bureau of Drugs, and the advancement of such men as Sam D. Finc. It is now clear all these men share the quality of integrity.

For Public Health Perspectives...

SINCE THE FOUNDING OF MEDICAL TRIBUNE, one of the primary elements in its credo was the need for public health perspective — to set our health priorities to accord with the incidence of death and disability. This made essential recognition that the two greatest potentials for reducing morbidity and mortality lay in reducing addiction to alcohol and tobacco. Beginning with its earliest issues, MEDICAL TRIBUNE pioneered in stressing auto safety and environmental pollution. These issues have now come from the backwaters of disregard to the mainstream of American consciousness with legislation and regulations for safer cars and a better ecology. Virtually no week or month has passed in which MEDICAL TRIBUNE has not also pointed the problems in the field of alcoholism and cigarette smoking. At long last a government regulatory agency has taken what is a first, but all-essential, step in an area where regulation can save scores of thousands of lives with simple, intelligent initiatives and non-prohibition, non-constrictive, constructive programs.



"... Had I known beforehand, I could have treated that chicken ..."

...Let All 'Show Their Colors'

NOW THAT THE BATTLE IS JOINED, we look to our leaders in Congress, to all members of the Senate and the House, to all officials in government to "show their colors." We fear that behind the scenes lobbying and pressures will be brought to bear on all branches of government. What is needed now is a mobilization of legislative as well as government leaders, of the scientific as well as the general community to support the FDA and, regardless of where the responsibility resides for the labeling, the advertising and the education of the public in respect to alcoholism, that it be honestly discharged and that effective action in respect to alcohol no longer be the exclusive province of vested, political and other interests.

MEDICAL TRIBUNE has never opted for prohibition. On the contrary, it has always favored a wide latitude of freedom of action. MEDICAL TRIBUNE has never opted for constrictive or prejudiced regulatory action. MEDICAL TRIBUNE has never opted for an unrealistic "informed consent" but rather for an intelligently and humanely informed public. We want no compulsory prohibition, no prejudiced, unrealistic regulation. We do want an informed public and realistic programs of action. When a problem is not honestly presented, there can be no constructive solution and, in the absence of a reasonable program of action, alcohol will continue to take its toll in the tens of millions—of its victims, of their families, and of the community of which they are a part.

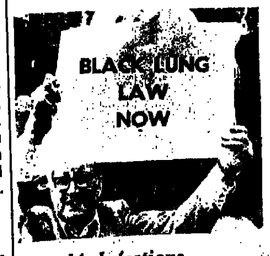
A.M.S.

LETTERS TO TRIBUNE

Black Lung Relationships

Your picture (MT, Oct. 15) struck me as being ironic in that the man holding the sign was demanding legislation and concomitantly smoking a big cigar.

OLIVER P. CAMPBELL, M.D.
Colorado Springs, Colo.



Anerobic Infections

Your article on anerobic upper respiratory infections was excellent (Infection Control Today section, MT, Nov. 5). This type of "reporting" is very worthwhile.

BERNARD MARCUS, M.D.
Somerville, N.J.

von Karajan

I read with great interest Dr. Sackler's interview with Herbert von Karajan on "Music and Medicine" ... I am also interested in work done on the international health front and W.H.O. in preventive medicine.

I am a psychiatrist but also a musician and greatly interested in art, film, dance, etc. — both intrinsically and for their value in therapy.

RUTH SCHNAPPER RINDER, M.D.
Milwaukee, Wis.

On the One Hand...

Your editorial [On the One Hand... (MT, Sept. 24)] was excellent. Unfortunately, I think it should have been in the *New York Times* rather than the MEDICAL TRIBUNE. One problem is that we are all very articulate in commenting on our problems in medical journals, but these comments never get into the lay press.

WARREN D. BOWMAN, JR., M.D.
Billings, Mont.

Beg Pardon

An advance notice (MT, Nov. 12) about an article in SEXUAL MEDICINE TODAY *(MT, Nov. 19) implied that Dr. Samuel B. Hadden achieves a heterosexual commitment in 80 per cent of the homosexual males whom he treats. The article itself correctly reported that commitment to a heterosexual life was "achieved in 30 to 40 per cent of selected patients."*

Our apologies to Dr. Hadden.

Sen. Kennedy Favors FDA Split to 2 Agencies

Continued from page 1

lawmaker told more than 500 leading physicians, investigators and drug company executives attending a national symposium on research standards.

Among the major reforms in his upcoming measure, Senator Kennedy reported, are plans to upgrade scientific recruitment, help facilitate release of new drugs, and provide for systematic feedback from the profession on experience with a new drug. His plans also call for creation of a National Drug Review Board composed of outstanding scientists who would have the authority to review—and, if necessary, over-rule—FDA decisions.

Keynote Speaker

The Senator was the keynote speaker at a meeting on Principles and Techniques of Human Research and Therapeutics jointly sponsored by Tulane University, the FDA and major pharmaceutical firms.

FDA Commissioner Dr. Alexander M. Schmidt, addressing another session of the meeting, said he concurred with many of Senator Kennedy's criticisms and goals but was opposed to splitting the FDA into two regulatory agencies. There is a "persuasive logic" to the FDA's present organization, he said, which enables it to mount agency-wide task groups to work on problems that cross bureau lines, and provide for a "consistent national approach" to similar legal and regulatory areas."

He asserted that "needed changes in FDA" could be effected by procedural revisions to help speed adequate drug testing and approval.

Senator Kennedy, in detailing his legislative plans for the agency, noted that the FDA is being asked "to do its job on a shoestring, with a budget that starves the agency and gives it totally inadequate manpower and resources."

"The current tasks of the FDA are overwhelming," he declared. "It must guarantee the safety and effectiveness of the nation's drugs. It must police a $100 billion group of private industries. It must see that drug production meets proper sterilization standards. It must guarantee that the nation's food supply is safe and uncontaminated. It must prevent cancer-causing substances from reaching the dinner table. It must protect the public against dangerous and defective heart valves, pacemakers, respirators and other medical devices. It must police the cosmetics industry and carry out a virtually endless list of other major responsibilities."

Serious Consequences

In the face of these massive mandates, the Senator continued, the FDA has "failed to attract and keep the top level scientific talent that it needs." One reason, he suggested, is that FDA scientists have no opportunity to do their own research. Another is that civil service salary limits make government service unattractive.

"The consequences are serious," Senator Kennedy observed. "Too often, FDA yields to the temptation to use caution and delay as substitutes for expertise and scientific judgment. Again, the public pays the price. Badly needed drugs are delayed from joining the fight against disease—not because they are dangerous, not because they are unsafe, but because of the agency's own well-deserved inferiority complex about its scientific judgment."

As for the FDA's advisory committees, he charged, "these permit the use of the scientist's name, but not always his full range of expertise." Advisory meetings are infrequent, short and "rely too much on summaries." "Seldom, if ever," the Senator said, "do all participants review the raw data on drugs they must approve. As a result, advisory committee decisions are too often rubber stamps for agency staff recommendations, rather than an independent review. The result can be disaster in the future, because we are papering over the fact that potentially dangerous drugs are being marketed with inadequate review."

Senator Kennedy's bill would mandate four major changes. It would:

- Set up a Drug and Devices Administration and a Food and Cosmetics Administration.
- Create, within the new DDA, a scientific division and an enforcement division, with a "significant proportion of the positions in the scientific division reserved for career scientists, and additional positions reserved for scientists who are not career employes." In addition, academic experts would be recruited to spend two- and three-year sabbaticals at the DDA and given decision-making responsibilities, and DDA career employes would be encouraged to spend sabbaticals at universities and other research environments.
- Give the DDA a "significant new authority"—a new " 'fourth' phase of the regulatory process" that would provide for "broad but carefully controlled distribution of a drug before final approval is granted." In this Phase Four concept, a drug might be limited to cardiologists, another to hospital-based physicians, a third to a particular region of the country. But all participating physicians would be expected to report systematically on their experience with the drug.
- Establish a National Drug Review

Continued on page 20

FDA overhaul is outlined by Sen. Edward M. Kennedy at New Orleans symposium sponsored by Tulane University, FDA and drug industry.

Clinicians Respond to Kennedy Proposal

Medical Tribune Report

NEW ORLEANS—Senator Kennedy's call for a massive revamping of the Food and Drug Administration met with qualified approval here from leading investigators.

Although none of the experts was prepared to endorse the Senator's package in toto, all of those queried by MEDICAL TRIBUNE in an informal spot-check of opinion were pleased that Congressional action was being proposed for what they saw as long-overdue reforms.

"Senator Kennedy's proposals will be among the most important contributions to the subject of drug development and drug regulation for the next five years," said Dr. Jerome Levine, Chief of the Psychopharmacology Research Branch, National Institute of Mental Health. "Mr. Kennedy has pinpointed problems that were only vaguely identified in the past, and his outline of proposed changes is certainly worthy of the most serious consideration. I was especially impressed," Dr. Levine added, "by the fact that he's going to ask for comment from all relevant sectors before he starts hearings on his bill."

Dr. Louis Lasagna, Professor of Pharmacology and Toxicology at the University of Rochester, had praise for Senator Kennedy's frankness in re-assessing the entire problem of FDA operations. "I think it's highly commendable that an important public figure should be saying openly that things are not well with the FDA," he declared. "Agency officials have been saying just the opposite for so long."

As for the Senator's specific proposals, Dr. Lasagna said that while he agreed with the lawmaker's analysis of "some of FDA's deficiencies," he was doubtful that the proposed reforms would necessarily solve the problems to which they addressed themselves.

"How will splitting the FDA into separate and independent agencies offer an answer to the need for recruiting competent scientific personnel?" he asked. He observed that the concept of Phase 4 monitoring was "attractive in theory, provided it's not an add-on to the present over-rigorous drug-approval procedures. If it's a tradeoff for earlier marketing of a useful drug, that would be all to the good."

'Over-Cautious'

Dr. George E. Bruch, Professor Emeritus of Medicine at Tulane University and an internationally recognized cardiologist, voiced approval of Senator Kennedy's efforts "to improve funding, staffing and operations of the FDA. "The agency has always been over-cautious," Dr. Burch observed, "As a result, good drugs take too long to reach the market. European physicians have excellent drugs that become available here only after long delay, propranolol or cromolyn, for example. Currently, beclomethasone is being withheld from American physicians. I believe that the Senator is trying to do the right thing. It could well be that his proposed separation of the FDA into two agencies would give members of the new drug agency more time, more specialized knowledge, offer them better preparation for their jobs."

A former division chief of the FDA, Dr. Elmer Gardner, now Chairman of the Department of Psychiatry, Washington Hospital Center, told MEDICAL TRIBUNE, "There's no doubt the FDA has suffered from lack of sufficient expertise in the areas for which it is responsible. The typical FDA scientist has to know all phases of medicine—research design and study, clinical practice, pharmacology and, to top it all, must know the drug industry. There's no such medical scientist anywhere in the world. There is practically no training for the prospective FDA physician. Too often, service with the FDA is, in a sense, punitive, not rewarding. The FDA physician is always under scrutiny by rival pressure groups—consumer, public, academia, industry."

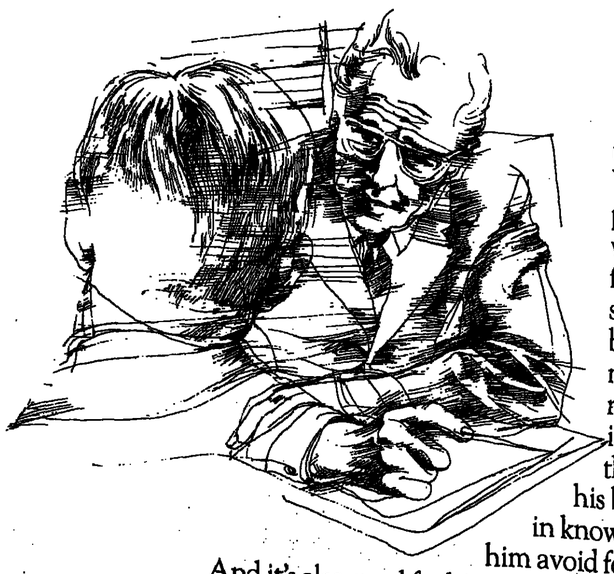
Dr. Gardner, who was Chief of the FDA Division of Neuropharmacology, commented that Senator Kennedy's proposal to split the agency could lead to better budgeting and staffing for the new Bureau of Drugs and Devices. But he cautioned that it could lead to a loss of the current centralization of some services in the field, making for less adequate field monitoring. He also warned that, unless the new agency provides adequate funding for sabbaticals and exchange programs, "We'll end up with more of a monster than we now have."

Dr. Leon Goldberg, Professor of Pharmacology and Physiology, University of Chicago, termed Senator Kennedy's approach "excellent," but questioned whether his proposals addressed themselves adequately to the problem of recruiting competent scientific personnel.

"I don't believe that the concept of two- and three-year sabbaticals is the answer," he observed. "How will the new agency go about recruiting scientists whose primary skills are in basic laboratory research? What will be the nature of the appeal? The problem is to define FDA's scientific base. The academic scientist might be persuaded to come on the basis of an appeal to his civic conscience, but once he is there, what influence will he have on decisions?"

"Let me tell you about the medicine I'm going to prescribe."

TALKING OVER VALIUM®(diazepam) THERAPY WITH YOUR ANXIOUS PATIENT



A patient often benefits by a greater understanding of his treatment program. You may find it helpful to make your patient aware that the purpose of therapy with Valium is to help reduce discomforting and disabling symptoms of excessive psychic tension and anxiety. It is beneficial for him to understand that much of his tension and anxiety can be relieved by your reassurance and counseling, and that these measures can do more than anything else to help him cope with his basic problems. The patient is reassured in knowing he can expect his medication to help him avoid feeling overwhelmed by his symptoms. And it's also good for him to realize that he will be taking Valium only as long as he needs it.

Your expressed confidence in the medication prescribed, and the positive atmosphere in which therapy is given and accepted, work to the patient's advantage.

"It's important that you follow my directions closely."

Selection of a dosage regimen is an important consideration when Valium (diazepam) is prescribed, and dosage should be individualized to achieve maximum beneficial effect. If the patient understands clearly when and how much to take, and if he knows why it's to his benefit to follow the regimen closely, the chances are better that he will take the medication precisely as directed. That should help avoid missed doses and discourage taking too much or too little medication — all of which can have an undesirable effect on the management of the patient's condition.

"I'll see you again the week after next and we'll see how you're making out."

Your patient is often likely to feel reassured when you talk about seeing him again to check his progress. A planned visit evidences your continued interest and affords the patient an opportunity to report improvement he has made and to relate whatever continuing or additional difficulties he may be experiencing. It's also a chance for him to describe his response to therapy with Valium.

During follow-up visits, as your patient talks about his medication and about its effects on his symptoms, he will provide the kind of information that will be of great help in evaluating total therapy, adjusting the dosage of Valium, or discontinuing the medication entirely if that seems indicated.

Valium® (diazepam)Ⓥ

2-mg, 5-mg, 10-mg scored tablets

for individualized treatment of psychic tension

ROCHE

Please see the following page for a summary of product information.

One Man . . . and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune

Say It Again, Sam*

OKAY, SO IT ISN'T *Poor Richard's Almanac*. But how many Ben Franklins do we really have? Statesman, scholar, printer, publisher, drafter of the Declaration of Independence, a bon vivant, full of wit and wisdom. In this day of specialization, when politicians are politicians with little wit and debatable wisdom, when our diplomats are schooled more in rhetoric than logic and their inventions relate more to what they believe than what they see, when our scientists number few statesmen and less bon vivants, thank goodness we still have a few men who specialize in pungent commentaries on the current scene—with wit and wisdom.

Sam Levenson is one such, and I have asked for his assistance in bringing to you a number of his observations which are related to the field of medicine, psychology and sociology. Sam said "Okay," so here we go. The captions are by *One Man . . . and Medicine* and the commentaries, incandescent, incisive and insightful, are by Sam Levenson.

On prognosis in the aged

I hope I'm really sick. I'd hate to feel like this if I'm well.

On taking medical history

My boy, I was sick before you were born.

On medical progress

If medical science has made so much progress in the last 50 years, how come I felt so much better 50 years ago?

On tinnitus

I beg your pardon, does the ringing in my ears annoy you?

On patient recall

At what point do you become an old-timer? You already are if you can remember:

When caster oil was the wonder drug.

When dope was what they called a less-than-bright youngster.

When doctors made house calls.

On Genetics

Insanity is hereditary . . . you can get it from your children.

On IQs

It has been said that a genius is a stupid kid with very happy grandparents.

A maternal glossary

1. High-IQ child: A kid who says dirty words earlier than other kids.

2. Autosuggestion: The parental compulsion to jump into (or in front of) an auto and get away from it all.

3. Hallucinations: See visions of kids without running noses.

4. Self-expression: In a child, any act which cannot be explained rationally.

5. Siblings: Children of the same parents, each of whom is perfectly sane until they get together.

6. Sex maniac: A husband who wants more children.

On child psychology

Child punishment, current American-style, runs somewhat along these lines:

About 6:15 pm, the mother gets very dramatic, turns to the child and says, "Go to your own room." He's got a television set there; he's got his own refrigerator; he's got a train set that goes through the other people's apartment and back again; they send his dinner in to him, leave him for the evening with an 18-year-old baby sitter—and he's being punished. His father didn't live like that on his honeymoon!

On the rights to privacy

There is a new rule which forbids parents from walking into their kid's room without knocking. The kid walks around with the Bill of Rights in his diaper and knows what he is entitled to. He's been advised by his four-year-old civil rights lawyer (the kid next door) that his lease entitles him to privacy.

On physical activities

You can't let a kid walk. He might get hit by a snowfluke and have a concussion. So the mother drives the child to the corner and keeps his body warm in the car until she can deposit him into the warm bus. By the time he gets to college he will need a course in remedial walking.

Paradoxical but true. The school spends $20,000 for a bus so the kids don't have to walk, and then spends $200,000 for a gymnasium so the kids can get exercise.

On prejudice

Some people are so prejudiced they don't even listen to both sides of a phonograph record.

Disliking people requires a reason; loving doesn't.

The difference between a conviction and a prejudice is that you can explain a conviction without getting angry.

On relative values

Papa was so impressed by a newspaper story reporting that Rin Tin Tin earned over $200,000 a year. "And we have to have children," Papa lamented.

On initiatives

Papa helped each of us get started on the road to success: "Remember, my son, if you ever need a helping hand, you'll find one at the end of your arm. And remember, too, if you want your dreams to come true, don't sleep.

On inflation

"A penny for your thoughts" is now 50 dollars an hour with the psychoanalyst . . . An apple a day costs more than calling the doctor. And if the doctor tells you you're sound as a dollar, you're really in trouble.

On orientation

Who said Columbus was an Italian? He was the first real American. When he started out, he didn't know where he was going. When he got here, he didn't know where he was. When he got back, he didn't know where he'd been. And he did the whole thing on borrowed money.

On nutrition

We have the best-fed garbage cans in the world, filled to overflowing with food that has been stabbed, cut, tasted and rejected. We throw away the skin, the fat, the gristle, the bone.

On anorexia

No one ever had to urge *us* to eat. (With our appetites, if you had put sugar on a fly it would have tasted like a huckleberry.)

On stimulating the appetite

My elegant brother Mike made Mama's left-overs sound gourmetish by giving them French names: hamburger accumulé, liver reclamé, ragout prolongé beef retourné, salmon rejuvenée, eggs renaissance.

On surgery and art

Mama bought a fresh whole chicken. Her daughter's chicken has been eviscerated, dismembered, neatly disjointed, frozen, and all its organs sorted out and filed in plastic see-through bags. The young housewife has been spared the bloody ordeal of chicken surgery. Chicken can now be bought in parts. Anyone can create his own version of a chicken out of a do-it-yourself chicken kit. Put together two heads, one eye, three breasts and four feet; add a mandolin, and you've got yourself an original poultry Picasso.

Prescribed for Waiting Rooms

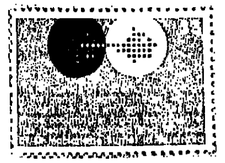
You sure can *Say That Again, Sam.*

We strongly prescribe several copies for the practicing physician's waiting room. We found the book a stimulant without side effects and a tranquiliser which sharpened the mind. Above all, patients under tension may very well appreciate its encouraging aspects and new perspectives on life. If your bookstore doesn't have it, let the Pocket Books people know you want it. Not all your medicine has to come in capsules or ampules. Here is a healthy treatment in inexpensive book form.

*Levenson, Sam: **You Can Say That Again, Sam; Pocket Books, 1 West 39th Street, New York, N.Y. 10018.**

Medicine on Stamps

Frank Macfarlane Burnet



Born in Australia in 1899, he received his M.D. from Melbourne University, joined Royal Melbourne Hospital, then decided to devote his life to research. After several years of study in England, he returned to Australia to stay. In 1942 he was elected a Fellow of the Royal Society and, in 1947, he received the Society's Royal Medal for his distinguished work in bacteriophages, viruses and immunity. His clonal selection theory of acquired immunity led to a Nobel Prize in Medicine in 1960.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

EPIGRAMS—Clinical and Otherwise

The real scientist . . . is ready to bear privation and, if need be, starvation rather than let anyone dictate to him which direction his work must take.
Albert Szent-Gyorgyi
in *Science Needs Freedom*
[World Digest, 1943]

Boost for Rabies Vaccine Seen in 'Interferon Inducer'

Medical Tribune Report

SALT LAKE CITY—University of Utah researchers have developed a technique that promises to increase the effectiveness of rabies vaccine. The method involves stimulating the release of interferon at the site of the rabies wound.

Dr. Burton Janis, Associate Professor of Medicine and Assistant Professor of Microbiology, and Maurice W. Harmon, a doctoral candidate in microbiology, report that mice exposed to rabies and treated with vaccine alone had four times the death rate of mice treated with a combination of vaccine and poly-I:C, an "interferon inducer."

Vaccine Blockage

"Human serum prevents the rabies virus from replicating until the body's own antibody response is activated," Dr. Janis said. "But the serum can also stall the body's own immune response by blocking the action of the vaccine. This is why booster shots of vaccine are necessary. We believe the use of an interferon inducer with the vaccine may be just as effective or more effective than serum and vaccine, with the added advantage that it would eliminate the need for booster shots."

Theophylline Monitored in Bronchospasm

Medical Tribune Report

ANAHEIM, CALIF.—To avert severe toxic reactions associated with the intravenous use of aminophylline in the treatment of acute bronchospasm, levels of serum theophylline should be carefully monitored, according to a report presented here at the 41st Annual Scientific Assembly of the American College of Chest Phsyicians.

Although aminophylline (a salt of the naturally occurring theophylline) has proved very effective in the treatment of acute bronchospasm, patients who receive it intravenously are sometimes subject to cardiac arrhythmias, seizures and even death, said Dr. Richard A. Matthay of Yale University School of Medicine. Control of asthma with aminophylline is best when serum theophylline levels are about 10 micrograms/milliliter while adverse affects are most common when the dosage is above 20 mcg/ml.

Chromatographic Assay

High pressure liquid chromatographic assay proved to be a rapid and practical method for monitoring serum theophylline levels in about 23 patients scheduled to receive intravenous aminophylline. In five patients with initial serum theophylline concentrations less than 10 mcg/ml, aminophylline dosage was calculated to raise the level to the accepted therapeutic range, said Dr. Matthay. Although they responded to therapy without ill effects, three out of four patients who received the usual dosage of aminophylline without having serum theophylline levels determined showed toxic symptoms.

Dr. Matthay pointed out also that the patients' prior history of aminophylline use correlated very poorly with theophylline levels and that continuous aminophylline therapy administered in a standardized dose of 0.9 mcg/kg/hour or less produced variable, and frequently excessive, serum concentrations of theophylline.

Based on his studies, Dr. Matthay proposes that carefully relating intravenous aminophylline dosage to serum theophylline may improve the outcome of therapy with that drug.

Tribune Economic Analysis

On Relocating The Urban Poor From Sick Cities

BY ELIOT JANEWAY
Consulting Economist

The urban crisis has festered to the point of precipitating a first-class financial panic. The time has come to start thinking about new solutions to the problem instead of just continuing to throw more money at the same victimized people.

Providentially, a different approach has been suggested by Dr. Bruno Bettelheim, the pioneering practitioner of reclamation techniques for the psychologically wounded at the University of Chicago. In an interview with me in 1969, Dr. Bettelheim pointed out that the American states boasting the biggest beckoning frontiers are hampered by having the smallest populations. Conversely, the smallest states are burdened with the greatest population congestion.

Until now, people with median incomes or better have been the ones taking advantage of opportunities to relocate from the country's congested areas, which are poor in natural resources, to its rich, undeveloped inland empires. Dr. Bettelheim's thinking calls for large-scale redistribution of the population to alleviate social pressures.

Picking up families on welfare in New York and just transplanting them en masse to New Mexico is not the answer. But asking what needs to be done to prepare the virgin lands of the West to absorb a planned population shift is the practical approach to a workable answer. Meanwhile, it makes no sense to waste dollars in keeping New York populated with slum dwellers while not using dollars to prepare New Mexico to overcome the disadvantages of being underpopulated. Bettelheim's concept targets the largest states that are hampered by the smallest population as the "sociological soil" in which to plant "seed money" for the building of new communities. A plan for orderly relocation offers the only long-term hope for the sick cities.

Ask Janeway

How can one open a Swiss bank account? Are there U.S. taxes on interest? Is such an account a good hedge against inflation?

Iowa Physician

Writing to the New York branches of the Swiss banks is one way. Whatever you deposit over there should be put on the table after tax savings have cleared IRS audits. All interest received is taxable, but your tax bill won't be much from a Swiss passbook because your interest will be so little. There are some worse hedges against inflation, but I can't think of them.

Send your questions on finances, investments, taxes to Janeway, MEDICAL TRIBUNE, 880 Third Avenue, New York, N.Y. 10022

Our Readers Write about the President's Cold Dr. Lasagna's Letter and Dr. Sackler's View

Continued from page 1

only the recommended symptomatic treatment and more often than not, the patients have to have subsequent visits because they become sicker and require antibiotics and sometimes hospitalization.

It is very reassuring and encouraging to me that a physician of Dr. Lasagna's reputation and expertise has spoken out on this matter.

WILLIAM G. GILLIES, M.D.
Galena, Ill.

THE WHITE HOUSE
WASHINGTON
November 18, 1975

Dear Harry:

Thank you for the most interesting yet controversial aspect of the President's recent cold.

Sincerely,

William M. Lukash, M.D.
Rear Admiral, MC, USN
Physician to the President

Mr. Harry Henderson
Editor-in-Chief, Medical Tribune
880 Third Avenue
New York, New York 10022

• I agree wholeheartedly with Dr. Lasagna! The FDA and HEW doctors should treat people, not computers.

DONALD B. J. LINDORFER, M.D.
Milwaukee, Wis.

• I refer to "colds" as "flu syndromes." These present with varying combinations of rhinitis, pharyngitis, adenititis, bronchitis, otitis media, myalgia, and malaise. Varied bacterial and non-bacterial complications are frequent.

When bacterial complications are likely, I always prescribe an antibiotic—usually tetracycline or erythromycin (or other antibiotics as specific treatment for various identified or suspected organisms, z.B., penicillin for Strep. infections).

When cough is present, usually this means that bronchitis is present, in the absence of findings to the contrary. I always treat bronchitis with an antibiotic—my first choice being tetracycline. It is my distinct impression that antibiotic therapy shortens the course of bronchitis associated with the "flu syndrome" in most cases.

There is no doubt in my mind that the expected benefits of antibotic therapy far outweigh the possible disadvantages of antibiotic side-effects which are seldom serious with the exception of penicillin sensitivity reactions which can be quite serious. Penicillin is actually the most dangerous of all antibiotics in common use, due to associated sensitivity reactions.

I prescribe mycostatin vaginal tablets for "as needed" usage for all mature females on antibiotic therapy for as much as 10 days or longer—due to the high incidence of monilial vaginitis in these patients.

LOYD C. BRANNON, M.D.
Athens, Ga.

• I concur one thousand per cent with the fact that generally speaking, patients with complications associated with "colds" visit physicians and therefore the majority *do* require the use of antibiotics. Possibly we should listen more to practicing physicians rather than "preaching" physicians.

ALLEN P. JETER, M.D.
Winnsboro, S.C.

• In January, 1974, I sent the enclosed pamphlet to all my patients and left copies in my office, available to anyone. My purpose was to provide information that would allow patients to care for themselves and become aware of those situations in which antibiotics might be of some value.

From discussions with my two associates and other colleagues in this area, I think that I can conclude that most patients in our practices are not seen for uncomplicated coryza and if seen for that problem are not treated with antibiotics. When needed, tetracycline hydrochloride and erythromycin sterrate are the antibiotics we most frequently use and the selection is usually made on the basis of several factors, not the least of which is individual physician preference.

Antibiotic overuse, like adverse drug reaction, is probably a figment of statistical imagination based on the extrapolation of unrealistic or incomplete studies.

Finally, I would like to thank you for your many valuable contributions to society.

AUGUSTUS A. AQUINO, M.D., P.A.
Bethesda, Md.

• May I say "bravo" for both Dr. Lasagna and Dr. Sackler?

As a solo private practitioner for 24 years, I haven't really had time to write letters to editors very often, but rather have used my time to make decisions about treating patients.

I agree completely with the statements made by both men.

CHARLES L. CUNIFF, M.D.
Jersey City, N.J.

• A tribute in your TRIBUNE to Professor Louis Lasagna for his astute observation that even the President does need treatment. A patient taught me how to treat a cold a long time ago: "If you had given me that penicillin yesterday, I wouldn't be sick today, so I'm not going to pay you for today."

We would have less trouble with critics if they would spend some time treating patients.

CLYDE H. DOUGHERTY, M.D.
Hopewell, Va.

• I heartily agree with Professor Lasagna's position on the "not so common cold."

Dr. Lukash did as so many of us in general practice have been doing for years since the advent of antibiotics, treating people with antibiotics after the first 3 to 5 days of home remedy have failed and seek our advice and prescriptions. After all, the bread winner has to be kept on the job, most children have to be kept in school and of course the housewife must be able to care for all of them.

When we read and go to seminars where the great professors tell us to avoid the use of antibiotics because colds are only viral infections, I always come home feeling guilty and for the next few days refrain from using antibiotics in the treatment of these "drawn out colds"—only to regret it later on when these same people call with a much more deep-seated infection or even pneumonitis.

So it is good to know that others are also using common sense in the treatment of these so-called "common colds."

CHARLES W. BURROUGHS, M.D.
Trenton, N. J.

• Many thanks for publishing Dr. Lasagna's letter.

As one of the many physicians in the area of primary care, I have often felt "defensive" after reading some article implying that I am abusing antibiotics every time I prescribe them. The next time I prescribe one, I'll bear down a little harder on the pen.

I am in a group practice, and I have CBC and culture availability in the office. This helps a lot, but when it comes to the daily decisions of when to use an antibiotic, all of the factors (cost, safety, chance of super-infection, indication of bacterial complication, duration of treatment, etc.) come into play every time we see the "uncommon cold."

JOHN A. MAPP, M.D.
Virginia Beach, Va.

• I am in the general practice of internal medicine and see many patients weekly similar to the situation described by Dr. Lasagna, and I am in complete agreement with him.

KEITH L. WRAGE, M.D.
Rockford, Ill.

• Dr. Lasagna is quite right when he says that most patients who arrive at our offices have already tried various nostrums for curing their colds. These people are, many times, complicated by a sinusitis and bronchitis or laryngitis. I rarely ever use antibiotics unless there is a definite evidence of bronchitis or any of the above.

At least this is my experience in my practice in a rural section of Virginia.

H. W. FELTON, M.D.
Deltaville, Va.

• Dr. Sackler's interesting article on "the common and not so common cold" stated, "What's good enough for the President of the United States is good enough for our patients, the citizens of the United States."

The entire article revolves around a much more critical issue than whether or not the President has a cold, but rather revolves around the issue as to whether or not those so-called armchair generals who have never seen or treated a patient making decisions regarding possible life-saving techniques that the practicing physicians have to deal with every day.

It is almost akin to armchair policemen making decisions six months later and still not coming to a successful conclusion as to what policemen have to make in split seconds, and criticizing them for the split-second decision that they had to make. Physicians likewise have to make decisions that are meant to be possible life-saving and yet must be able to withstand the criticisms from those who have never had to make a single decision in this respect.

It was a fine, thought-provoking article.

MAYNARD J. AMELON, D.O.
Detroit, Mich.

Dr. Lasagna Writes on Colds and Antibiotics

March 27, 1974

Dear Arthur:

One of the most constantly raised points in the current discussion about overprescribing of drugs is the alleged prescribing at a spinal reflex level of antibiotics for "the common cold." It is repeatedly said that in surveys of doctors in practice, a very high percentage of patients who come to the doctor's office for "the common cold" receive an antibiotic.

On the face of it, this seems reprehensible. On reflection, however, it occurs to me that most patients do not visit a doctor's office, and pay good money, for advice about uncomplicated coryza. I suspect, instead, that most patients with upper respiratory complaints go to see doctors suffering from a combination of cough, stuffed nose, post-nasal drip, swollen glands in the neck, earache, etc.—in other words, from secondary bacterial complications of the common cold. If this is the case, then the prescribing of an antibiotic is not wrong; rather, the question is only: what antibiotic would be best?

I ask that you print this letter in Medical Tribune to solicit from your readers some facts bearing on the statements I have just made. If I am wrong, then the doctors of this country deserve the severe criticism they are receiving from many quarters at present. If I am right, then the doctors are practicing good medicine, and it is the critics who deserve disapproval.

Louis Lasagna, M.D.

Reprinted from MEDICAL TRIBUNE, *Nov. 19, at request of Dr. A. M. Sackler*

Atherosclerotic Plaque Lowered By Cholestyramine

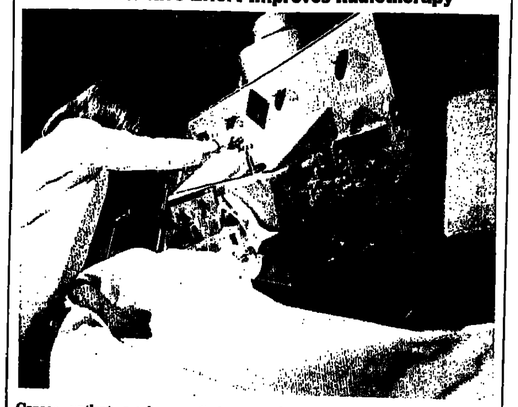
Continued from page 1

Morphologic measurements of atheromatous lesions in drug-and-diet treated rhesus monkeys showed that progression of disease had not only stopped, but that there had occurred a "substantial decrease" in the luminal narrowing of the coronaries and "very marked reductions" in the lesion mass of aortic plaques, following a year's treatment, Dr. Wissler reported. Studies by means of labelled cholesterol also demonstrated "a rather remarkable decrease" in both free cholesterol and cholesterol esters in the [aortic] lesions," he said.

In reporting the studies, part of an ongoing investigation on the potential for regression in atherosclerosis, Dr. Wissler stressed that the current findings were made in plaques produced in a relatively short time by an extreme atherogenic diet. Uncompleted research now underway, he reported, is seeking to determine the possibilities of regression in the non-lipid, collagenous portions of plaques typical of long-term atherosclerosis.

The experimental animals in the cholestyramine study were 24 rhesus monkeys, about five years old, who were fed a high-cholesterol, high-fat diet to induce severe atheromatous plaques within 12 months. The diet consisted of ordinary monkey chow enriched with 2% cholesterol and 25% fat. At the outset of the study, all of the monkeys were comparable in serum cholesterol concentration, with levels in general less than 200 mg %. These rose to a peak of 800-1000 at nine months and were at approximately 750 mg % at the end of one year when five of the monkeys were killed and autopsied to serve as a reference group.

Collaborative Effort Improves Radiotherapy



Cancer patient receives radiotherapy via betatron, administered by a member of the new Cancer COM-RAD Network in New York. A collaboration of nine major metropolitan medical centers, the network uses computers to improve the quality, the design, and delivery of radiotherapy to cancer patients. COM-RAD is based at Mt. Sinai Hospital.

The remaining animals were divided into four groups and followed for an additional year. Group II was maintained on the atherogenic diet, Group III was fed a low-fat, cholesterol-free diet, Group IV received the same diet combined with cholestyramine, and Group V was continued on the atherogenic diet but also received cholestyramine.

'Remarkable Drop'

Among the highlights of the findings, Dr. Wissler declared, were these:

- Cholestyramine added to the atherogenic diet produced a "remarkable drop" in serum cholesterols to about 250 mg %.
- The drug did not lead to a significantly lower serum cholesterol when added to the low-fat low-cholesterol ration, but it "did sustain what appears to be substantially more regression."

When all of the monkeys were killed at the end of two years, morphologic studies showed "a virtual absence of gross aortic lesions" in some of the animals treated with the combined drug-and-diet regimen, compared with the reference group.

Fat-staining of the plaques showed "even the most severe of the aortic lesions of the three treated groups contained very little lipid (intracellular or extracellular) and showed no evidence of a necrotic center, features that were prominent in both of the untreated groups of aortas," Dr. Wissler reported.

Coauthors were Drs. Dragoslava Vesselinovitch, James Borensztajn and Randolph Hughes.

Kennedy Favors Division of FDA Into 2 Agencies

Continued from page 13

Board, with two full-time chairmen and a full-time staff, the outside members to be exempt from civil service salary limits.

The Massachusetts lawmaker said that because of the profound changes called for by his proposals, he would postpone hearings on the legislation until next spring but would meanwhile ask for assessments of the proposals and recommendations from the American Society for Clinical Pharmacology and Therapeutics, the National Academy of Sciences, the Pharmaceutical Manufacturers Association and others.

Dr. Schmidt proposed three procedural changes, some calling for enabling legislation, to help speed drug approval. The first calls for FDA-industry agreement on a study design before any drug trials are undertaken. In past practice, Dr. Schmidt noted, "FDA generally took the position that we would review material when it was submitted and then give our opinion... This approach was not mere nastiness, although it was a bit unfair. It was based on the view that drug development was 'their' business, drug review was 'our' business, and we would lose our objectivity if we participated in a study design."

'Staged Approval'

The FDA chief's second recommendation urged "staged approval" or "continued and sequential review" of trial data submitted by a drug company, so that "at any given time, all interested parties know how the tally sheet reads —what their score is and whether they are winning the game."

A major bonus of sequential review, Dr. Schmidt said, is that once a company knows its ongoing studies are approved, it would be able "to invest the large sums required for the remaining clinical research (related to safety, dosage, etc.) without worrying overly that the FDA, in a late stage of the game, will point out a fatal defect."

Dr. Schmidt's third recommendation, not dissimilar to Senator Kennedy's, calls for a more flexible approval system, coupled with a systemic feedback procedure about physician experience with a drug after marketing.

"The greatest single weakness of our present regulatory system is the abysmal reporting by almost all professionals about their drug experience—good, bad or indifferent," Dr. Schmidt declared. He urged that the FDA be given authority to resume studies of a drug after it has been marketed, and to approve drugs for restricted use, for example, "only in a hospital, only by certain specialists, or only by physicians who had taken a specific period of training or would agree to report results in a particular manner."

"In effect," he concluded, "these changes might permit earlier appearance in the United States of many drugs, in return for a longer investigational phase controlled by FDA. This seems to me a reasonable tradeoff."

Severity of Cervical Cancer Underestimated?

Medical Tribune Report

PHILADELPHIA—Sizable numbers of cervical cancer patients are now being classified as having microinvasive disease when their condition has actually reached a more serious stage that requires radical hysterectomy.

This is the conclusion of investigators at two medical centers, who recommended adoption of a new definition of microinvasive disease here at the American Cancer Society's National Conference on Gynecologic Cancer.

Drs. Hervy E. Averette, of the University of Miami School of Medicine, and James H. Nelson, of the Downstate Medical Center, Brooklyn, pointed out that the current definition of Stage 1A disease includes penetration of cancer cells to a maximum depth of 5 mm beneath the basement membrane.

Instead, they propose that all patients with infiltration of cancer cells into the stroma to a depth of more than 1 mm should be considered as having invasive Stage 1B disease. Only disease with less than 1 mm penetration, not accompanied by vascular or lymphatic involvement, should be considered microinvasive and be treated by simple removal of the uterus alone, they said.

Their new definition is described in the American Cancer Society publication "Dysplasia and Early Cervical Cancer," which they coauthored with Dr. Ralph M. Richart, of the Columbia University College of Physicians and Surgeons.

Dr. Averette commented that medical literature does not provide enough data to define microinvasive disease adequately, but in his opinion 5 mm of invasion is "definitely too much— that's halfway through the cervix."

Problems with Pathologists

Problems also arise, he added, because pathologists frequently do not measure precisely the depth of penetration into the stroma.

In surveying published accounts of cases of carcinoma of the cervix, Dr. Averette found information on 198 patients treated by radical hysterectomy with pelvic lymphadenectomy. A majority of the reporting investigators specified that depth of invasion had been limited to 5 mm, yet eight of the patients (4 per cent of the total) were observed at surgery to have metastasis to lymph nodes.

Dr. Averette compared these findings with data collected over the past decade at the Miami and Brooklyn medical centers on 162 patients with Stage 1A cancer of the cervix, defined as penetration of less than 1 mm without vascular or lymphatic invasion. None of these patients has shown nodal metastasis or recurrence of disease, he emphasized.

To be safe, therefore, the Florida investigator would limit the Stage 1A category to patients with a maximum penetration of 1 mm. He believes that anyone else should have radical surgery including removal of the pelvic lymph nodes, supportive tissues of the uterus, and the upper vagina. Ovaries would be left in young women. Such surgery carries a mortality risk of 1%.

Acknowledging that the stand he advocates might seem overly conservative, the investigator agreed that choice of treatment of patients with cancerous penetration between 1 and 3 mm into the basement membrane is still controversial. It has not yet been conclusively determined, he said, whether these patients require radical measures.

Vein Grafts Aid Pre-Infarction Angina Patients

Medical Tribune Report

ANAHEIM, CALIF.—"A relatively high percentage" of patients treated by emergency vein-grafting for pre-infarction angina resistant to medical therapy "can look forward to improved prognosis and a normal existence," according to Dr. Cary J. Lambert of the Baylor University Medical Center.

Sixty-one of 95 patients treated by means of aortocoronary bypass were symptom-free, fully productive and not taking medication for angina two-and-a-half to five-and-a-half years postoperatively, Dr. Lambert told the 41st Annual Scientific Assembly of the American College of Chest Physicians.

In addition, 18 other patients consider themselves subjectively better and, at 30- to 67-month follow-up, are under control with anti-anginal medication, Dr. Lambert said. Six inhospital deaths were ascribed to peri-operative myocardial infarctions. Two deaths were attributed to left main lesions and another to a trapped septal perforator. Three patients died prior to surgery.

Of seven survivors with peri-operative infarctions, five are alive and symptom-free, two have medically manageable angina and none have congestive heart failure, Dr. Lambert asserted. Seven "late deaths" were caused by myocardial infarction, hepatitis, pulmonary embolus, cerebrovascular accident and suicide.

Pointing out that several investigators have attested to the high early mortality and guarded long-term prognosis in patients who develop pre-infarction agnia, Dr. Lambert said: "The overall survival of our surgically-treated group at an average follow-up period of 32 months is 86%. It is to be noted that three of our operative deaths occurred as a result of operating upon a recently infarcted ventricle.

"We feel that greater diagnostic acumen and new methods of diagnosis such as the myocardial scan may differentiate evolving infarctions from impending infarctions and thus avert exposing acute infarctions to the increased risk of early surgical intervention.

"All in all, we conclude that direct surgical intervention has a place in the management of patients with pre-infarction angina, particularly when these patients continue to have inhospital angina."

Steroids May Be Detrimental In the Treatment of Hepatitis

Medical Tribune Report

CHICAGO—Corticosteroids, commonly used in the treatment of severe viral hepatitis, do not contribute to survival and even may be detrimental, a group of California investigators told the American Association for the Study of Liver Diseases.

A prospective double-blind randomized trial of methylprednisolone showed that more patients died on the corticosteroid treatment than on placebo, although the difference was not quite statistically significant.

"Fifty percent of the patients assigned to methylprednisolone died during the 16 week study and only 13 per cent of those assigned to placebo died," said Dr. Peter B. Gregory, Assistant Professor of Medicine in the gastroenterology division of Stanford School of Medicine.

Major criteria were chosen to select seriously ill patients. No patient was admitted to the trial if symptoms were present for less than three months. Fourteen patients received methylprednisolone and 15 were given placebo. Dose was 48 mg daily divided for four weeks with a taper to 12 mg at the end.

Initial liver biopsies were obtained in 14 patients before entering the study and as soon as possible after beginning treatment in the remaining 15. All biopsies were coded and interpreted by three observers without knowing the clinical history.

Bridging necrosis was seen in 13 of the placebo group and in 11 of the corticosteroid group. Histologic findings were comparable in the two treatment groups. Two of the placebo group died and seven of the corticosteroid group. Serious side effects of steroid were a contributory cause of death in one patient.

"Follow-up biopsies in those who survived and completed the 16-week study demonstrated chronic active hepatitis in five of eight patients on placebo and one of three patients on methylprednisolone," said Dr. Gregory.

He recommended that the use of corticosteroid for severe viral hepatitis be discontinued until further studies confirm or refute the results.

Clinical Trials

By Oldden

TRIBUNE SPORTS REPORT

Pain in the Athlete's Heel

By DR. PETER SPERRYN
Hon. Secretary, British Association of Sports and Medicine

Special Tribune Report

MANY of the sportsmen's most disabling medical problems are of simple causation and respond to simple remedies, once the cause is understood.

Pain around the heel is frequent in all sports and a moment's pause to consider both footwear and sporting environment will help to put the clinician on the right diagnostic track.

The commonest of the heel disorders are surely blisters due to ill-fitting shoes or failure to wear socks. The simplest—though cruellest—treatment of blisters is simply to de-roof them, to put on spirit [alcohol] or Friars' Balsam [compound benzoin tincture] and then raw Elastoplast [adhesive elastic bandage preshaped to fit the heel].

In this way the irritant effect of a sliding lint dressing is averted and the sportsman can resume his activity forthwith. When shoes are sufficiently ill-fitting, or the underlying calcaneum is sufficiently prominent, persistent friction may lead to the formation of superficial or deep calcaneal bursae which lie respectively superficial and deep to the achilles tendon insertion at the back of the calcaneum.

Apparent on Saturday

The diagnostic problem is that in many sportsmen the diagnosis may be fairly apparent on Saturday evening, with a reddened fluctuant swelling in the affected area, but may by Monday or Tuesday show little abnormality. Bursae usually respond to a spell of rest, especially if protective padding of ring type can be devised to avoid further direct pressure on the lesion.

Quite often barefoot running is an excellent temporary measure. Thereafter hydrocortisone injection after aspiration may help some to settle down and a small minority give persistent symptoms leading to surgical cure.

Calcaneal bruising is quite common in certain events, most especially in long jumpers and triple jumpers in athletics where a fairly hard take-off board is vigorously struck. Similar lesions are seen in any sportsman who trains or performs on a very hard surface, especially in poorly padded shoes.

The diagnosis is made on the history and confirmed by the finding of tenderness on the postero-inferior aspect of the calcaneum.

Physiotherapy methods such as short-wave and ultrasonic may be of help here if available but like any periosteal bruising, considerable time may be required for the lesion to settle satisfactorily.

Heel Cups Help

Adequate padding with Sorbo, Plastazote or similar materials can be beneficial and pre-formed plastic heel cups are available to fit inside sports shoes and these can alleviate symptoms by spreading the stresses on the heel more evenly.

Hydrocortisone injections are usually unrewarding in these situations.

It should be remembered that the fat pad under the calcaneum may become dissipated when the fibrous dividing strands become weakened or disrupted by repeated mechanical insult, so that the athlete loses the natural protection of his own heel pad.

Nothing can restore this anatomically, so padding is a useful prophylactic measure.

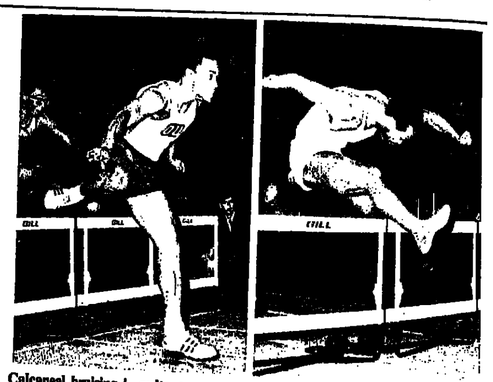
The outside possibility of a stress fracture of the calcaneum should not be forgotten in cases of severe or chronic exposure to injury and an X-ray may occasionally be required.

Calcaneal fractures are usually dramatic events following directly upon violent injury, usually a direct fall from a height on to the heels, as may be seen in parachute jumpers.

Calcaneal spurs are often found on X-rays and, in the best medical traditions, blamed for any symptoms that happen to be localized to the lower side of the calcaneum.

As calcaneal spurs are such a common finding, it has always been difficult to assess their role in relation to symptoms. It is likely that the majority of spurs are harmless and best left alone. Certainly standard treatment of most of the lesions around the heel leaves the bony spur intact while relieving the symptoms.

Further forward on the anterior inferior limit of the calcaneum and in the soft tissues immediately adjacent to it is the tender area found in plantar fasciitis.



Calcaneal bruising is quite common among hurdle jumpers and other athletes who perform or train on very hard surfaces while wearing poorly padded shoes

This is commonly brought about by running on a hard surface in scantily padded shoes and probably reflects repeated stress of the longitudinal arch during the thrust phase of running.

It can be differentiated from spring ligament strain quite simply because in plantar fasciitis there is well localized tenderness very near to the heel, whereas in spring ligament strain the pain is further down the foot and more directly related to the middle of the anatomical arch.

Simple plantar fasciitis will respond rapidly to rest and heel padding, but if this fails within two weeks then there is no point in delaying hydrocortisone injection which is gratifyingly effective in the vast majority of cases.

Physiotherapy methods very rarely improve on the time-scale. Spring ligament strain may be treated by foot exercises, sometimes requiring faradic footbaths for preliminary education of the athlete in correct use of his intrinsic foot muscles and by attention to some instep support if the shoes are obviously inadequately constructed.

Applications Are Being Accepted for Johananoff International Fellowship

Medical Tribune World Service

MILAN, ITALY—Applications for the Johananoff International Fellowship for Advanced Biomedical Studies for 1976-1977 are presently being accepted by the Mario Negri Institute for Pharmacological Research in Milan.

The award is presented each year to a distinguished scientist for outstanding contributions in one of the following fields: cancer chemotherapy and immunology; cardiovascular pharmacology; neuropsychopharmacology; or drug metabolism.

Last year's winner was Dr. Herbert S. Schwartz, cancer research scientist at Roswell Park Memorial Institute in Buffalo, N.Y. He received the fellowship on the basis of his original research on the factors involved in cytotoxic actions an antitumor drugs.

Under the terms of the award, Dr. Schwartz is spending one year at the Institute in Milan investigating the factors and mechanisms determining the selective cytotoxicity of agents which interact directly with DNA, altering its structure in specific target cells.

DNA-reactive drugs, recently introduced into cancer treatment, include adriamycin and daunorubicine. Both are anthracycline antibiotics.

Dr. Schwartz' main objective is to prepare a comprehensive review which will assemble and evaluate already existing knowledge in his field.

Applications for the 1976-1977 award should be airmailed no later than January 28, 1976 to The Johananoff Fellowship Committee, Instituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea, 62, 20157 Milan, Italy.

IMMATERIA MEDICA

Soul Disco Hypertension

For reasons that we still can't understand, we were drawn into a Lexington Avenue music store where we stood gawking. Then we saw something that made us decide that that was why we came. It was a 45 rpm record called *Hypertension*, distributed by Buddha Records, written and conducted by Paul L. Kyser. We bought it.

"Do you know what you're doing?" asked the salesman. "That record just came in five minutes ago and you walk in and buy it. Two sides, both *Hypertension*. Do you know what you're getting?"

"No, but you have to be with it, man. Hypertension's my thing," we responded, which is the only way out of a situation like that. Just be cool.

On Part I...

We took it home and played it. On Part I there were lyrics; Part II stuck to the instrumental. The beat was steady throughout—much like a heartbeat, we told ourselves. On the instrumental side, things steadily got more cacophonous, pressury, wildly electronic and even, we'd say, twangy in an Oriental rock way. We took it up with our musician-in-residence. "Soul disco," he said. "*You* bought that?" He fainted dead away.

But our greatest problem lay in the lyrics. We couldn't understand them part of the time and when we did, we couldn't connect them with hypertension, renin, sphygmomanometers, salt or anything else we normally look for.

Talking to Paul Kyser

Instead, we got on the phone and finally, with the help of Michael Milrod of Buddha Records, we were talking to Paul L. Kyser, the composer and leader of the Calendar group that recorded the music. He turned out to be a 27-year-old musician who had studied at Rutgers and with the late Hal Weiss, an arranger for the Ed Sullivan show. In eight years, Kyser has had two records in the "million-seller" class and 15 hits. One was *Body and Soul, That's the Way It's Got to Be*, which is not to be confused with the original song; the other was *Ain't It Good Enough?* Among his other hits were *My Ebony Princess* and *Where Were You When I Needed You?*

So we explained we needed him because we didn't "get" the lyrics on *Hypertension*. He laughed and said, "Look, there's two kinds of hypertension. There's the kind my mother has. That's medical hypertension—I forget what her blood pressure is but it's really sky-high. But that's medical hypertension and if you get all worked up and upset you can get that kind.

"And then there's another kind of hypertension—and that's when people, like all my friends, have tension and pressure. Everything's frantic, uptight, it's the schedules, the timetables, the deadlines, the landlord, the traffic, everything pouring in on you. A lot more people have this hypertension, this pressure due to the way they're working and living. You get excited. It gives you headaches. You're all wound up. It affects the rich and the poor. It's all around me—and that's why I love writing songs. They're about me and my people, everyone I know. I love writing a message in my songs."

He ran hastily through the lyrics for us, clarifying what the singers' phrasing sometimes blurred, and promised to send us a lyric sheet. We thought we understood things a little better.

It would make a lot of sense, we mused, since the incidence of hypertension among black people is so high, for the National Heart and Lung Institute to underwrite some real hypertension blues and rock just to reach all those young people who never turn up for screening or treatment. *Dear Ted Cooper*, we began . . .

Clearing Things Up

But to get back to the lyrics, when we got Paul Kyser's lyric sheet, we at last understood a great deal. The song is titled *Hypertention*—not *Hypertension*. This is why Paul Kyser was talking about two kinds of hypertension. What he said was now perfectly clear. And this is why his lyrics, so inexplicable to us at first, go:

Well, well, well, well,
let me be, I gotta be me,
who puts me through this misery

I work all day 'n drink all night
trying to make the situation right
my destiny's on a shaky course,
just as shaky as the job
I just lost

My baby brother is in jail,
'n I'm out here trying
to hustle up his bail,
My landlord is bugging the (beep)*
outta me
and I feel like I'm gettin'
HYPERTENTION, don't you
mention
HYPERTENTION, don't you
mention
HYPERTENTION, don't you
mention
HYPERTENTION, don't you
mention
HYPERTENTION, don't you
mention

℗ *Pi Kappa Records*

So you can see what a typo can do, even when created by a sharp copy-editor who knows how to spell hypertension. That's hypertention, a new entity, and as they say in *Reader's Digest*, life in these United States.

*Beep—hell